A CLINICAL STUDY OF FUNGAL RHINOSINUSITIS

Dissertation submitted

In partial fulfillment for the award of

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CERTIFICATE

This is to certify that this dissertation titled "**A CLINICAL STUDY OF FUNGAL RHINOSINUSITIS**" has been prepared by **Dr. A. KARTHIGA** under my supervision in the Department of Otorhinolaryngology, Government Stanley Medical College & Hospital, Chennai during the academic period 2010-2013 and is being submitted to the Tamil Nadu Dr.MGR Medical University, Chennai in partial fulfillment of the University regulation for the award of Degree of Master of Surgery (M.S Otorhinolaryngology) and her dissertation is a bonafide work.

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DECLARATION

I **Dr.A. KARTHIGA**, Solemnly declare that the dissertation, titled **"A CLINICAL STUDY OF FUNGAL RHINOSINUSITIS"** is a bonafide work done by me during the period of FEB 2011 to SEP 2012 at Government Stanley Medical College and Hospital, Chennai under the expert supervision of **PROF.DR.M.RAMANIRAJ, M.S., D.L.O.,** Professor and Unit Chief , Department Of Otorhinolaryngology, Government Stanley Medical College and Hospital, Chennai.

This dissertation is submitted to The Tamil Nadu Dr. M.G.R. Medical University in partial fulfilment of the rules and regulations for the M.S. degree examinations in Otorhinolaryngology to be held in April 2013.

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CONTENTS

INTRODUCTION

The Kingdom of fungi is ubiquitous and omnipresent having prevailed over the tides of time, over numerous decades by adapting to various methods of survival in the susceptible host including humans. Estimates vary, but the number of fungal species probably exceeds 50,000 and most benefits mankind.

Fungi of saprophytic form derive nutrition from decaying organic matter. These forms increase in virulence when the host is immunocompromised.

Fungal Rhino sinusitis is a known medical entity seen in the ENT Out Patient department. Acute or Chronic Rhino sinusitis is a common condition affecting upto 20% of population of which 6%-12% is caused by fungi. Fungal Rhino sinusitis presents as Acute/Chronic and Invasive/Non-Invasive based on duration and Histopathological evidence of Invasion into Sinonasal sub-mucosal tissue.

The presenting signs & symptoms of Acute or Chronic Fungal Rhinosinusitis are not distinctly different from those seen in Bacterial Rhinosinusitis. Patients usually compliant of purulent rhinorrhea, persistent headache, facial pain, diplopia, nasal polyp, nasal obstruction. A high index of suspicion clinically should be supported by histopathology in the diagnosis of fungal infections.

Invasive Fungal Rhino sinusitis unless diagnosed early and treated aggressively can lead to Intracranial or Intraorbital complication & has a high mortality rate.

In the current study, we evaluate the epidemiology, wide spectrum of clinical manifestation, Histopathological characteristics & the best methods for accurate diagnosis of Fungal Rhino sinusitis.

REVIEW OF LITERATURE

1. HISTORICAL PERSPECTIVES
2. TAXONOMY OF FUNGI
3. RELEVANT ANATOMY OF NOSE & PARANASAL SINUSES
4. ETIOPATHOGENESIS
5. CATEGORIZATION OF FUNGAL RHINO SINUSITIS
6. CLINICAL MANIFESTATIONS
7. STUDY REVIEWS

1. HISTORICAL PERSPECTIVES:

A. In 18th century Plaignaud described 'Fungal tumor' in Maxillary sinus of a 22yr old soldier

B. Oppe defined Aspergillus sp. was the causal factor for sinusitis in 1897 in a patient with infection of sphenoid sinus. The disease in that patient had extended to involve the cerebrum through erosion of the bone.

C. Mackenzie in 1894 described what is probably the first case of apparent non-invasive fungal sinusitis

D. Hora in 1965 recognized 2 categories of Fungal Sinusitis- Invasive & Non-Invasive

E. Baker et al in 1957reported for the first time, an acute fulminant type of Fungal Rhino sinusitis caused by Zygomycetes in immunocompromised patient.

F. Milosev et al first recognized the chronic granulomatous type of Invasive Fungal Rhino sinusitis in sudan in 1969.

G. Finby & Begg did the documentation of the benign entity of fungal ball or sinus mycetoma in 1972.

H. Ponikau et al in 1999 using novel diagnostic techniques showed fungi & Eosinophils in 96% of Chronic Rhino Sinusitis & coined the term Eosinophilic Fungal Rhino sinusitis (EFRS).

I. In 1976, Safirstein isolated Aspergillus sp. from sinus cultures of patients with polyps and found that the clinical picture of these patients was similar to the findings observed in Allergic Bronchopulmonary Aspergillosis (ABPA), a benign allergic process.

J. Robson et al in 1989 replaced the term as Allergic Fungal Sinusitis for Allergic Aspergillosis as the condition was caused by a number of fungi.

2. TAXONOMY OF FUNGI

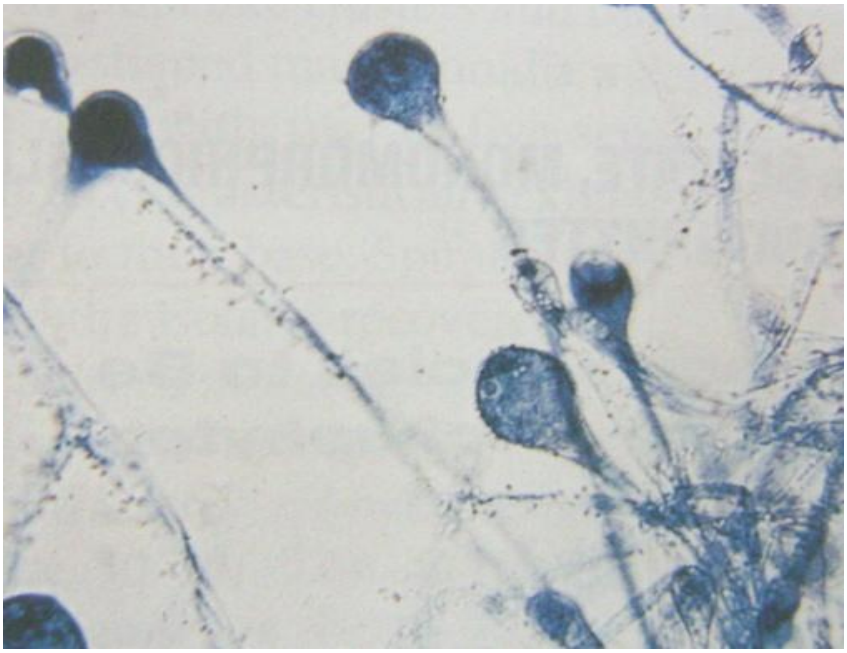
Fungi are closely related to bacteria – Actinomycetales & Nocardia asteroids which are transitional types. Actinomycetales branch like fungi but also assumes bacillary & coccoid forms. Nocardia stains acid fast like tubercle bacillus. The unique property of fungi – Dimorphism exist both as spore & mycelia form. Fungi are Eukaryotes & each fungal cell possesses atleast one nucleus & nuclear membrane, endoplasmic reticulum, mitochondria & secretory apparatus. They are obligate or facultative aerobes.

Taxonomy:

Taxonomy of fungi is very confusing due to recent problems of precise identification of specific organisms. As per Manning et al, fungi are classified into pathogenic, saprophytic & usual lab contaminants that rarely infect humans.

Zygomycetes:

Hyphae of the Zygomycetous have very distinctive characteristics. They tend to be of large diameter (10-15um) & only sparsely septate. Hyphal branch angles often are at 90 degree, but sometimes can be at 45 degree as well. **Genera:** Absidia, Cunminghamella, Mucor, Rhizomucor, Rhizopus.



Rhizopus species are the main cause of Acute Invasive Fungal Rhino sinusitis.

Ascomycetes:

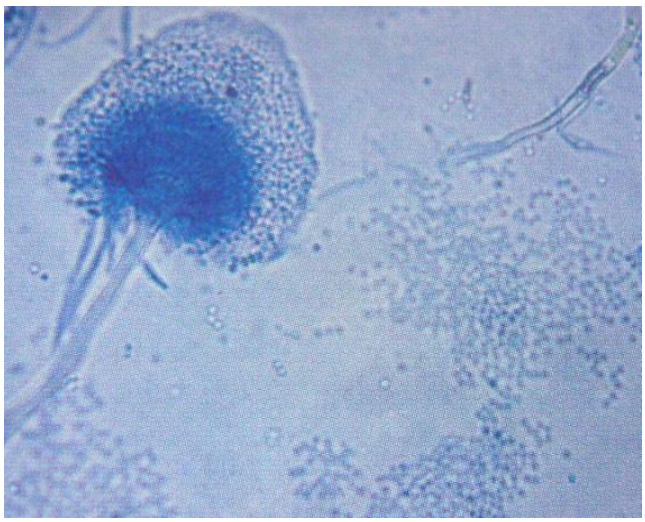
Hyphae of Ascomycetes form septa regularly in conjunction with growth and non-pigmented (hyaline). They are also called dimorphic fungi – both yeast & hyphae forms exist. **Genera:** Candida-yeast, Histoplasma, Blastomyces, Trichophyton, Microsporum, Pseudallescheria boydii, Scedosporium prolificans.

Deutromycetes:

Hyphae are septate. They are of two varieties – Dematiaceous (Pigmented) & Hyaline (Non-pigmented).

Dematiaceous – Alternaria, Curvularia, Bipolaris, Cladosporium; Infections caused by dematiaceous moulds are called Phaeohypomycosis. Feature of these moulds commonly seen in sinusitis is that many of their hyphal cells are enlarged & globose in shape.

Hyaline – Aspergillus, Fusarium, Penicillium, Scedosporium; Infections caused by hyaline type are said to be hyalohyphomycosis (colourless hyphal mycosis). Aspergillosis is the best example of hyalohyphomycosis.



Aspergillus often exhibit hyphal branch angling at 45 degree & hyphal tips that branch into 2 parts of approximately equal length. Aspergillus & Fusarium can cause either Invasive or Non-Invasive.

DIFFERENCE BETWEEN ASPERGILLUS AND MUCORACEAE:

ASPERGILLUS	**MUCORACEAE**
Narrow ,hyphae 45 degree angled branching Septate hyphae	Broad ribbon-like hyphae 90 degree angled branching Aseptate hyphae

3. RELEVANT ANATOMY OF NOSE & PARANASAL SINUSES:

The following aspects of the Anatomy of Nose & PNS are relevant to Fungal Rhino sinusitis.

Lateral Nasal wall:

Inferior turbinate & Inferior meatus:

It is the largest of the three turbinates. It is a separate bone, the inferior which has an irregular surface, perforated and grooved by vascular channels into which mucoperiosteum is firmly attached. The turbinate possesses an impressive submucosal cavernous plexus with large sinusoids under autonomic control which provides the major contribution to nasal resistance. Nasolacrimal duct opens into the Inferior meatus.

Middle turbinate:

The middle turbinate has a visible projectile portion in the nasal cavity and an invisible portion transversing the ethmoid labyrinth. It has 3 parts namely the Anterior 1/3rd , Middle 1/3rd & Posterior 1/3rd. The Anterior 1/3rd is sagitally oriented and attached superiorly at the junction of cribriform plate and the lateral lamella . The Middle 1/3rd runs posteroinferiorly across the Lamina papyracea & the medial wall of Maxillary Antrum giving a vertical phase to the ground lamella of

middle turbinate in the coronal plane. In its posterior 1/3rd the attachment of the ground lamella turns to run horizontally to reach the crista ethmoidalis of the perpendicular plate of palatine bone. The ground lamella of Middle turbinate separates the anterior ethmoid cells from the posterior ethmoid cells, which has to be penetrated during endoscopic sinus surgery to enter the posterior ethmoid. The posterior end of the middle turbinate forms the anterior boundary of the Sphenopalatine foramen through which the Sphenopalatine artery enter into the nasal cavity. Maxillary sinus drains into the Middle meatus.

Uncinate process:

It is a boomerang shaped bony process running parallel to the Ethmoid bulla, which together bounds the Hiatus semilunaris. The Hiatus leads into the 3 Dimensional space, the ethmoidal infundibulum bounded laterally by the Lamina Papyracea & medially by the Uncinate process. Inferiorly the bony attachment of Uncinate with the Inferior turbinate may be dehiscent leading to the formation of the fontanella of Accessory ostia of Maxillary sinus.

The Superior attachment of the Uncinate may be variable. In majority of cases, it is attached to the Lamina papyracea laterally terminating the Ethmoidal infundibulum into the recess terminalis. In the remaining 15% of individuals it may be attached to the skull base

superiorly or to the middle turbinate medially, in which the frontal recess continues into the Ethmoidal infundibulum.

Bulla Ethmoidalis:

It is the largest & consistent air cell of the anterior ethmoid. It may not be pneumatized & bony in 8% of individuals called conus bulla. Superiorly the bulla may extend upto the roof, that is called fovea ethmoidalis or may stop short of fovea. The space between the fovea and bulla is called the suprabullar recess. Posteriorly the bulla may extend upto the ground lamella or may be separated by the retrobullar recess. Laterally the bulla is bounded by the Lamina papyracea.

Posterior Ethmoid cells:

The posterior ethmoidal cells are 1 to 5 in number bounded by basal lamella anteriorly, anterior phase of sphenoid posteriorly and lamina papyracea laterally. These cells drain into superior meatus. The posterior most cell of the posterior ethmoid may sometimes pneumatize extensively, posterosuperiorly & laterally into the sphenoid sinus, such cell is called as onodi cell. The optic nerve may come in close relation to the lateral wall of onodi cell. Hence the optic nerve may be inadvertently injured during the Endoscopic Sinus Surgery in the direction of the sphenoid sinus.

Sphenoid sinus:

Sphenoid sinus show variations in size & shape, as well as position & direction of the intersphenoid septum. The anterior wall of sphenoid sinus is approximately 7cm from anterior nasal spine. The roof of the sphenoid sinuses presents as convex bulge corresponding to the roof of the pituitary fossa. The upper lateral wall is related to the optic nerve, more posteriorly & inferiorly, the lateral wall is related to the Internal Carotid Artery.

Frontal sinus:

Frontal sinus pneumatization is highly variable from Agenesis to extensive pneumatization called pneumosinus dilatans. Frontal ostium & frontal recess resembles an hourglass shape.

Frontal Recess:

It is bounded medially by the middle turbinate, lateral wall of the olfactory mucosa, laterally by lamina papyracea, posteriorly by anterior ethmoid artery, suprabullar recess & bulla.

4. ETIOPATHOGENESIS:

Numerous environmental & host factors are responsibe for the development of fungal sinusitis.

Veress et al postulated that hot and dry climate favors chronic nasal inflammation, resulting in tissue damage followed by immunologic reaction of the host to fungal antigens.

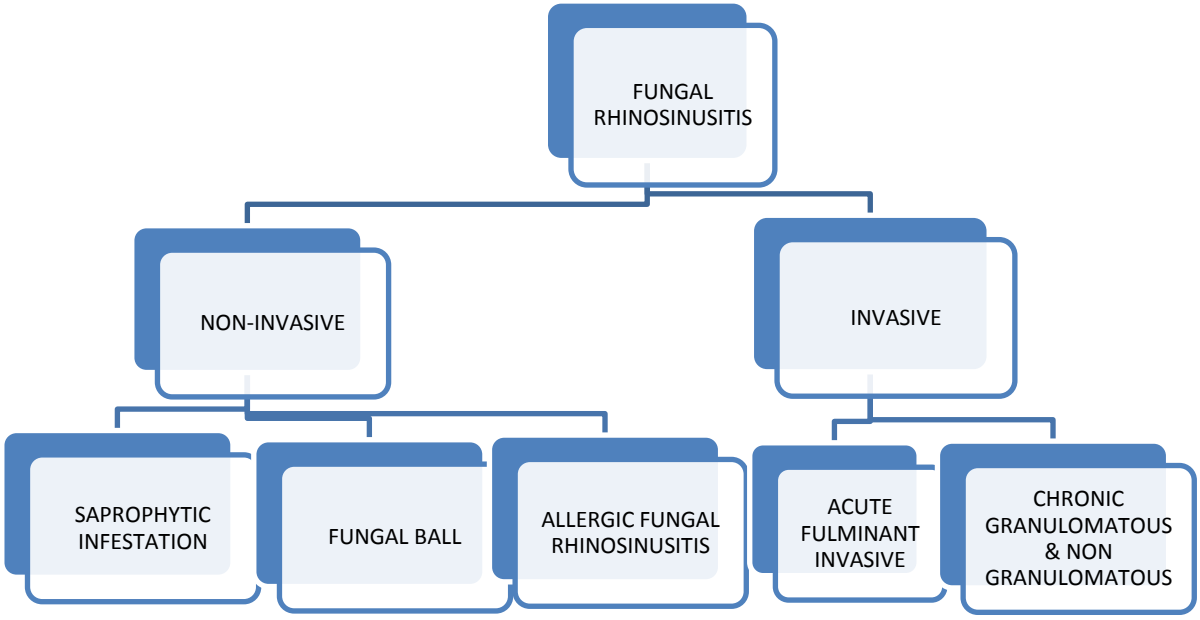
Allergic mucosal thickening has a strong predisposing effect on development of Aspergillus & dematiaceous fungal sinusitis.

Other factors are long term steroid (local/systemic) use, chronic bacterial sinusitis, host factors such as diabetes mellitus, carcinoma, blood dyscarias, immunodeficiency states & local anatomic variations.

Axelsson et al (1910) evaluated underlying factors in their series of fungal sinusitis & found that number of patients had been on prolonged antibiotic therapy for sinusitis.

Stammberger believed that local anatomic factors in middle meatus produces obstruction & predispose patient to bacterial infection. The resultant mucosal change, ostial obstruction, decreased ventilation lowers the pH & thereby favors the fungal growth.

5. CATEGORIZATION OF FUNGAL RHINO SINUSITIS:

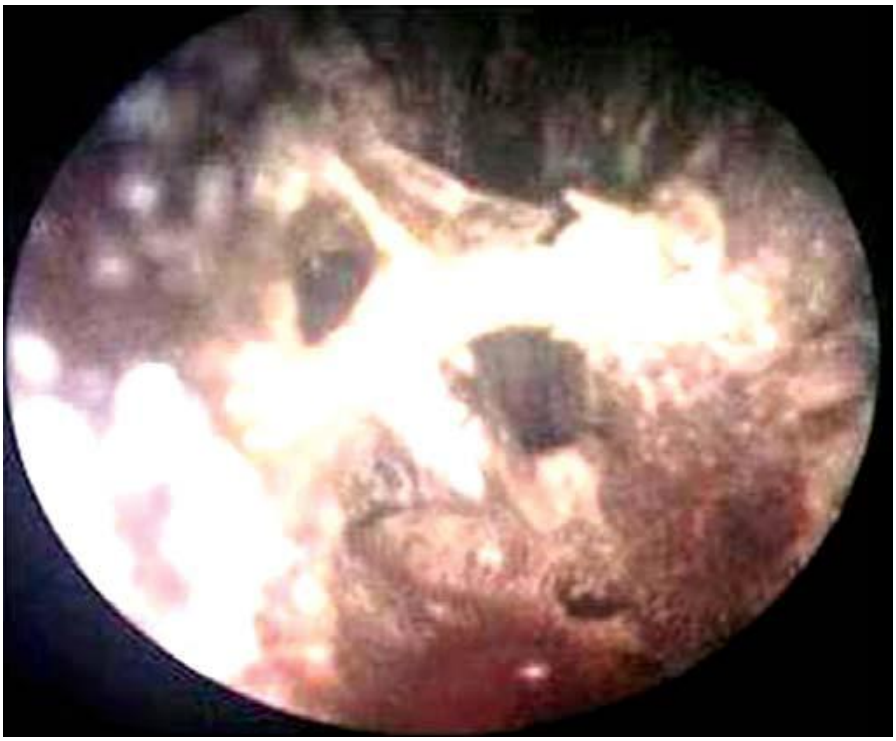


Host defence	Immunocompromised	Immunocompetent	Atopic
Fungal form	Invasive	Saprophytic Fungal Ball Granulomatous	AFRS

Invasive Fungal Rhino Sinusitis:

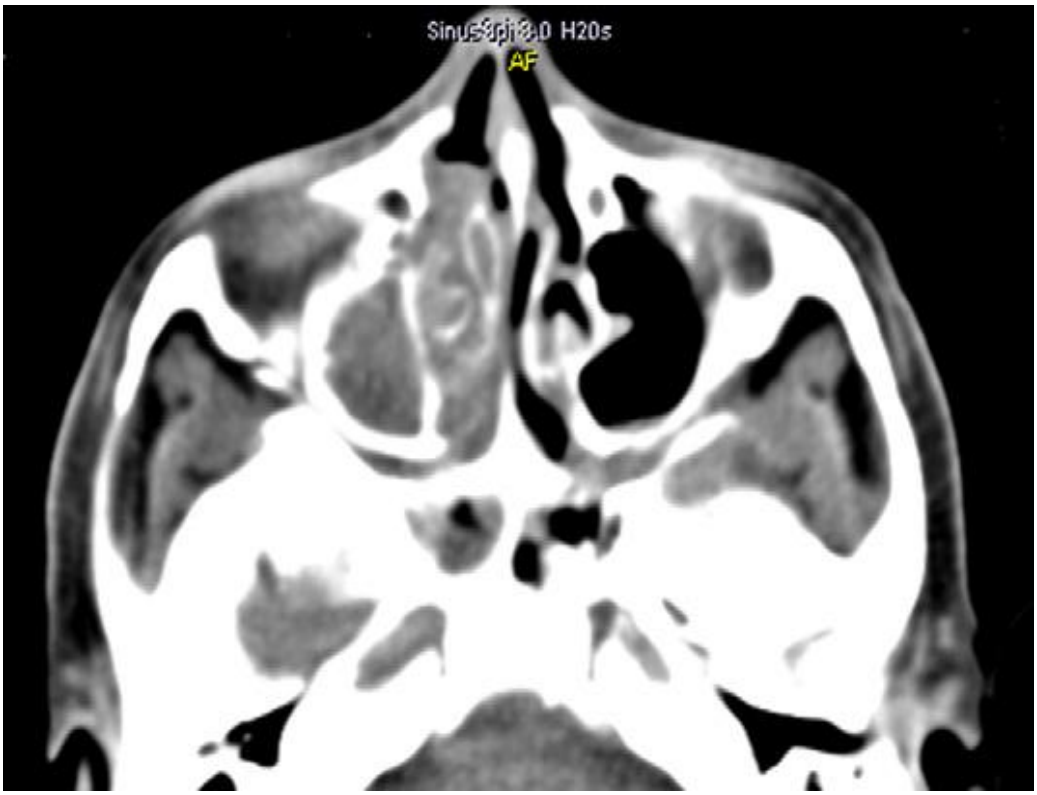
Acute Fulminant Fungal Sinusitis:

Commonly caused by members of the class zygomycetes or by Aspergillus. This disease occurs more often in the immunocompromised patients & associated with a mortality rate exceeding 50%. Histopathologic examination shows hyphal forms within the submucosa with or without Angiocentric invasion and tissue necrosis with minimal host inflammatory cell infiltration. The role of a high index of suspicion coupled with meticulous nasal endoscopic evaluation makes for an accurate diagnosis, which may be life saving. The bone destruction & soft tissue swelling occur in advanced disease in imaging studies.



An endoscopic image of the left nasal cavity, showing complete obliteration with dense, black eschar-like crusts.

Endoscopic image of the right nasal cavity, showing blackening and crust formation of the right middle turbinate and middle meatus, the biopsy of which showed mycotic tissue invasion, and the KOH mount showed fungal elements.



Picture showing Unilateral Acute fulminant invasive fungal rhinosinusitis, invading to all sinuses on the same side. Bone erosion & mucosal edema is also seen.

Chronic Granulomatous Invasive Fungal Sinusitis:

This disease has been primarily described in Sudan, India, Pakistan & Saudi Arabia characterized by a time course of more than 12weeks. Symptoms may develop once the orbit or the skull base are involved. Proptosis is the most common presentation of cases from sudan. Invasion of maxillary floor may produce palatal erosion. Although Aspergillus species were identified as the causative agent, other varieties has been associated such as Mucor, Alterrnaria, Curvilaria, Bipolaris.

Histopathology showed eosinophilic material surrounded by fungus, giant cells and palisading nuclei, variable number of lymphocytes and plasma cells.

Chronic Non-Granulomatous Invasive Fungal Sinusitis:

This entity is a slow destructive process that commonly affects the ethmoid and sphenoid sinuses but it may also involve other sinuses. The disease typically follows a time course of >12weeks. In contrast to chronic granulomatous Invasive form, Granulomatous invasive type is characterized by tissue necrosis with little inflammatory infiltrate and dense hyphal accumulation resembling fungal ball. It is usually common among immunocompromised patients but also seen in immunocompetent individuals. Aspergillus fumigatus is the common agent isolated.

Granuloma formation, fibrosis, vascular proliferation, scanty fungal infiltration, absence of vascular invasion, isolation of Aspergillus flavus & geographical restriction are probably the important differentiating features of granulomatous type from Non-granulomatous type of chronic invasive fungal sinusitis.

Non-Invasive Fungal Rhino Sinusitis

Localized fungal colonization (Saprophytic infestation):

Asymptomatic colonization of mucus crust with in nasal cavity by

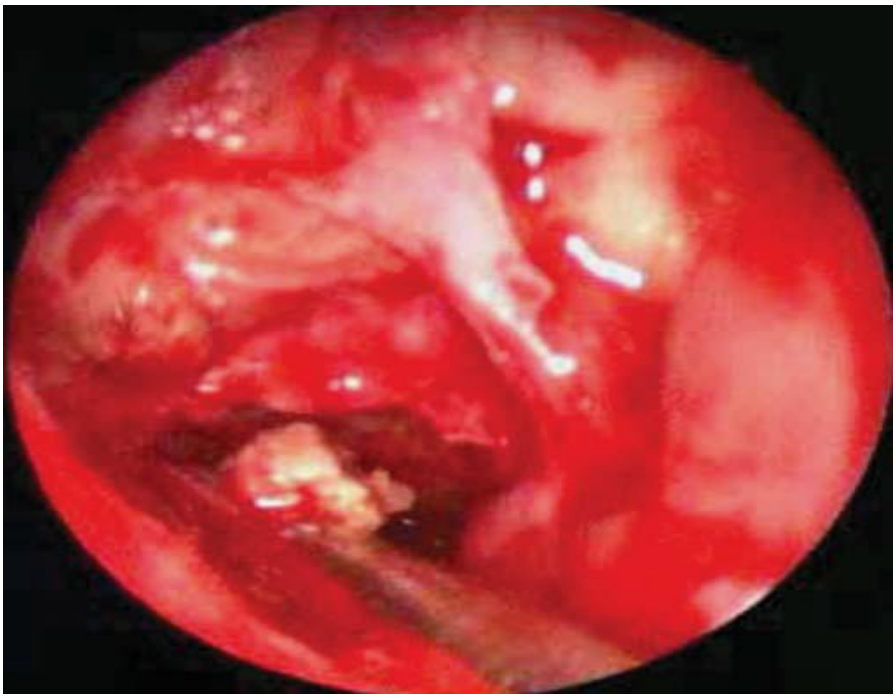
fungi, often seen in patients who had previous sinus surgery. Most patients have a benign course & treatment may not be warranted in such colonization.

Fungal ball (Sinus Mycetoma/Aspergilloma of sinuses):

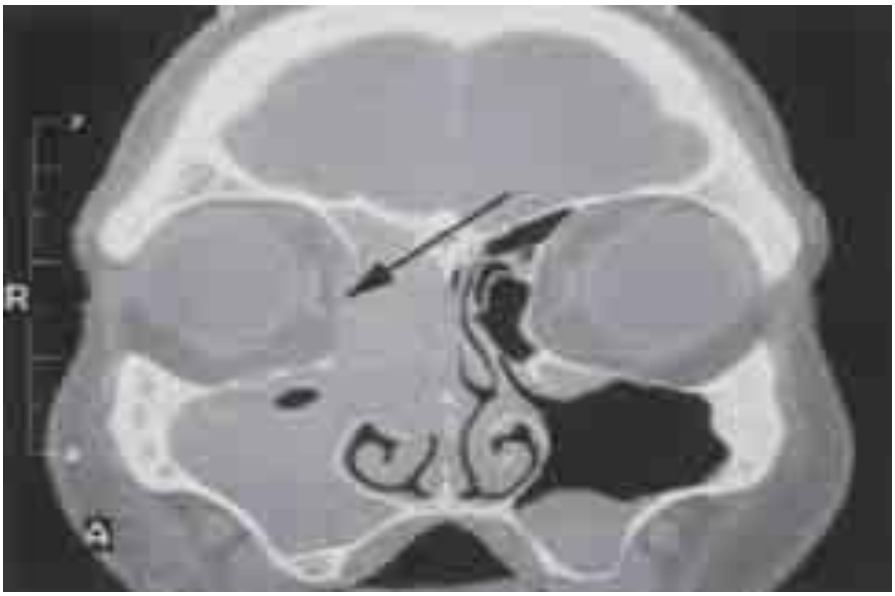
Fungal ball of the paranasal sinuses are composed of matted fungal hyphae. The host is immune competent. Cultures are frequently negative and the diagnosis is based on the characteristic Histopathological examination. Histopathology: fungal balls are extra mucosal fungal infestations. The fungi usually can be seen on routine hemotoxylin and eosin stains. A tangled mat of hyphae is present.

Causative organisms – Aspergillus fumigates, Aspergillus flavus, Alterrnaria species. Only 23-50% cultures result in fungal growth.

Endoscopic photograph showing a fungus ball in the left sphenoid sinus.



Endoscopic intraoperative image of a fungal ball being evacuated from the right sphenoid sinus.



Coronal section shows complete opacification of the right ethmoid sinus with a partial bone lysis (arrow), and a partial opacification of the right maxillary sinus.

Axial CT – PNS showing an isolated right maxillary sinus opacification, with reactive sclerosis of the bony margins. The patient was found to have fungal mass within the right maxillary sinus on surgery, making the final diagnosis of a right fungal ball.

Coronal CT – PNS showing right sphenoid sinus opacification, with disease in the lateral recess of the right sphenoid sinus, in close proximity to the foramen rotundum and vidian canal. The patient presented with a right sided headache, which was relieved after an endoscopic evacuation of the right sphenoid sinus, with the KOH mount of the evacuated material showing fungal mycelia.

Eosinophilic related Fungal Rhino Sinusitis:

1. Allergic Fungal Rhino Sinusitis:

Bent & Kuhn proposed Diagnostic criteria for entity of Allergic Fungal Rhino Sinusitis:

a)MAJOR CRITERIA

A) Type I (IgE Mediated) Hypersensitivity

B) Nasal Polyps

C) Characteristic CT findings

D) Positive Fungal stain or Culture.

E) Allergic mucin with fungal elements and no tissue invasion.

b) MINOR CRITERIA

A) Asthma

B) Unilateral predominance

C) Radiographic bone erosion

D) Fungal culture

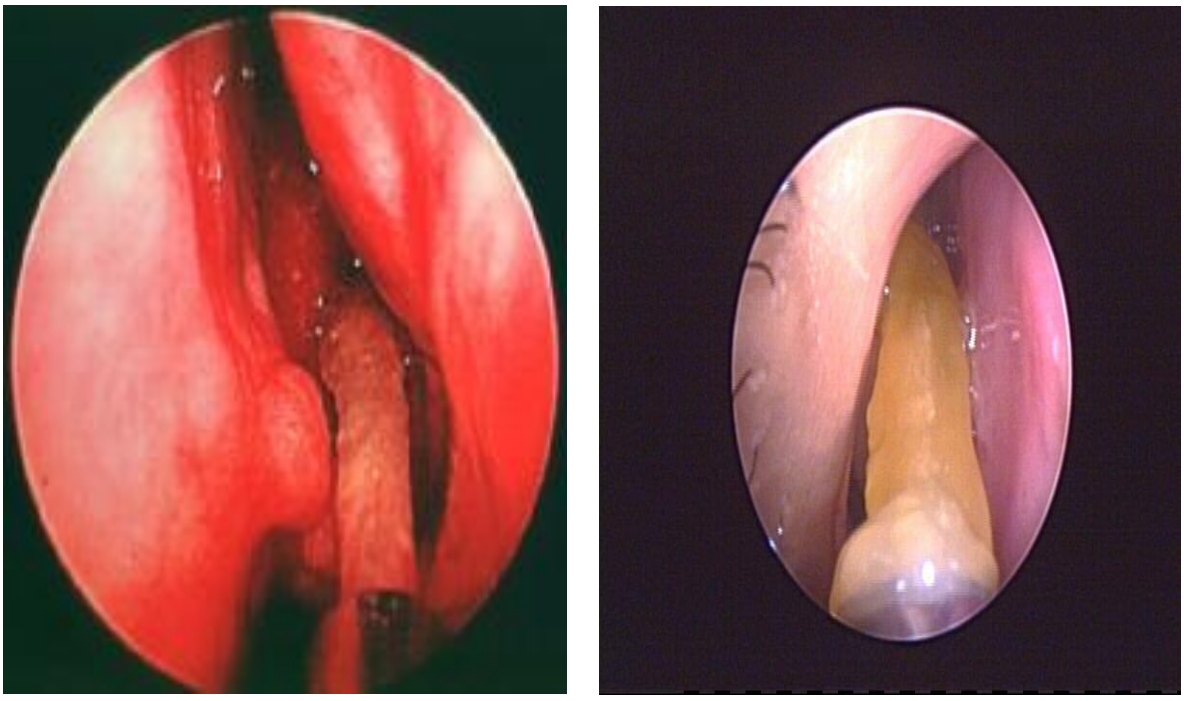
F) Charcot Leyden crystals

G) Serum Eosinophilia

The ‘peanut-butter’ or ‘cottage-cheese’ like mucin evacuated from sinuses of patients of Allergic Fungal Rhino Sinusitis is indistinguishable from the mucoid impactions of patients with Allergic Broncho Pulmonary Aspergillosis. Termed Allergic mucin, is tan to green; brown to black; consists of whole & partially degenerated eosinophils, Charcot-Leyden crystals, sparse hyphae & mucus. The allergic mucin seen containing the maximum load of fungal elements which are known to have a great affinity for calcium, manganese, magnesium & other ferromagnetic substance. However the most important aspect in the concept of Allergic Fungal Rhino Sinusitis is the allergy (Type I Hypersensitivity) to fungi. The presence of fungal allergens, incites a Gell and Coombs type I and Type III inflammatory response. The resulting obstruction of sinus ostia and stasis in the sinuses creates a favorable environment for growth of fungi . The slow accumulation of allergic fungal mucin over a period of time resembles a mucocele . Bone remodeling and decalcification may occur, making the disease to mimic invasion into adjacent anatomic spaces. The location of bone demineralization and extension appears to be determined by expansible disease process that occurs as a result of combination of pressure and local inflammatory mediators. This process often gives rise to facial dysmorphism, exophthalmos, and intracranial extension.

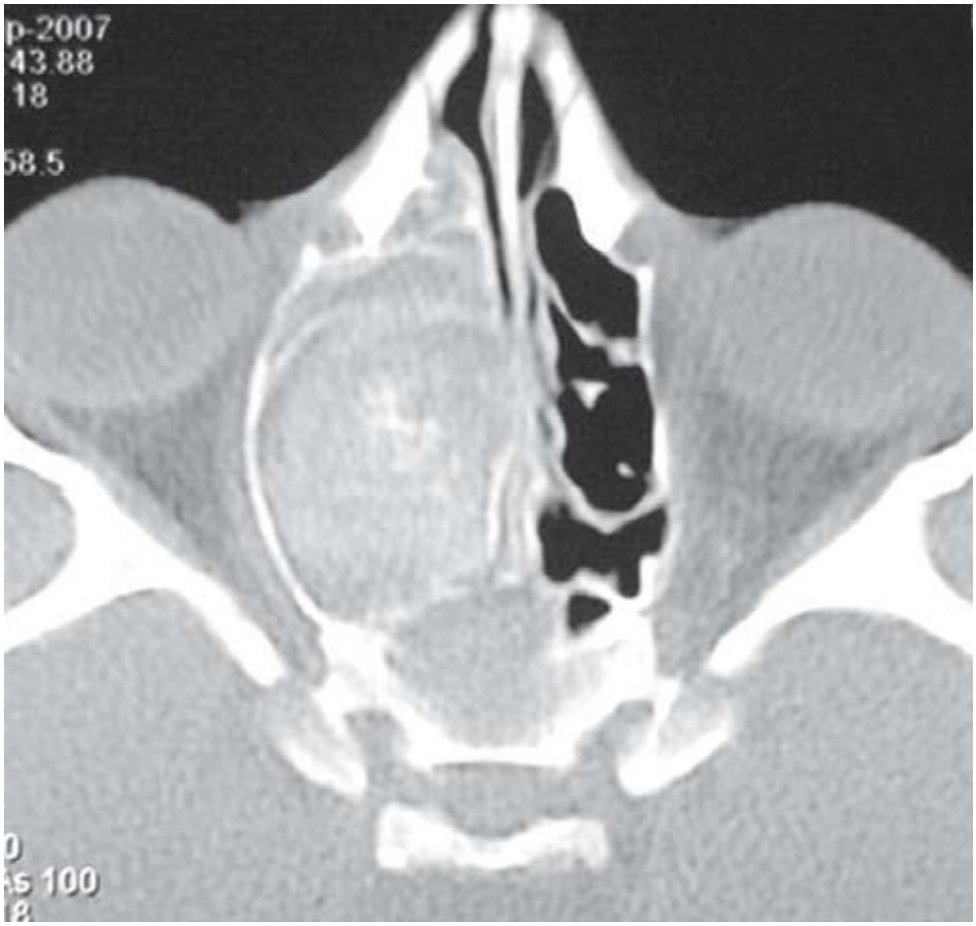
Characteristic CT findings include characteristic heterogenic opacification of involved sinuses which has been named as starry sky pattern, ground glass appearance or serpeginous patterns, but commonly referred as double density sign, which is best appreciated in soft tissue window & this corresponds to areas of hypo density on T1 weighted MR images & signal void on T2 weighted MRI.

Causative Agent: Demitaceous fungi (Alternaria, Curvilaria, Bipolaris, Drechslera, Exserohilum, Chrysosporium)

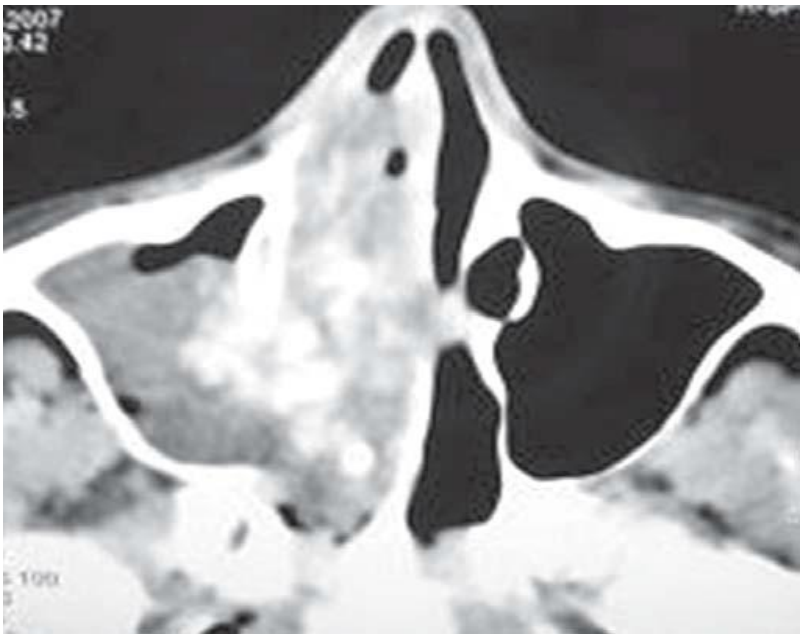


Suctioning of thick allergic mucin.

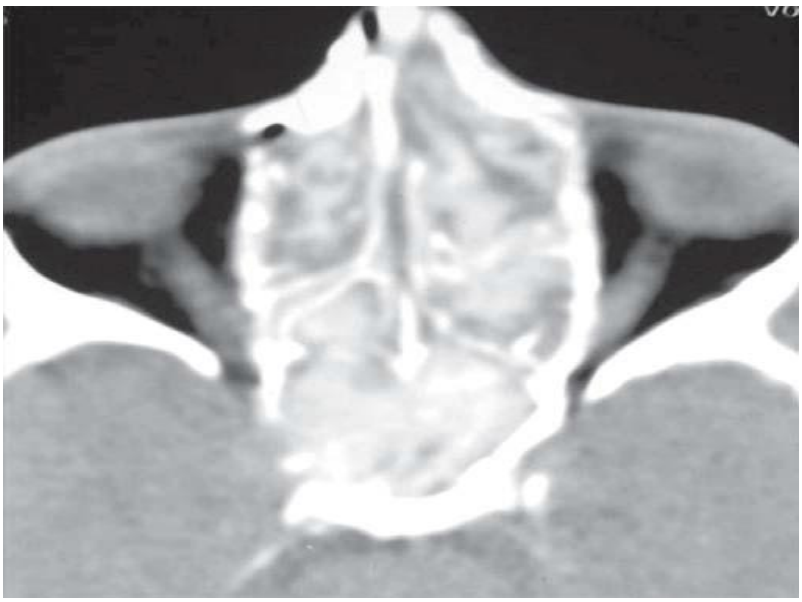
Nasal endoscopy images of fungal colonies occluding the osteomeatal complexes along with polyps and allergic mucin.



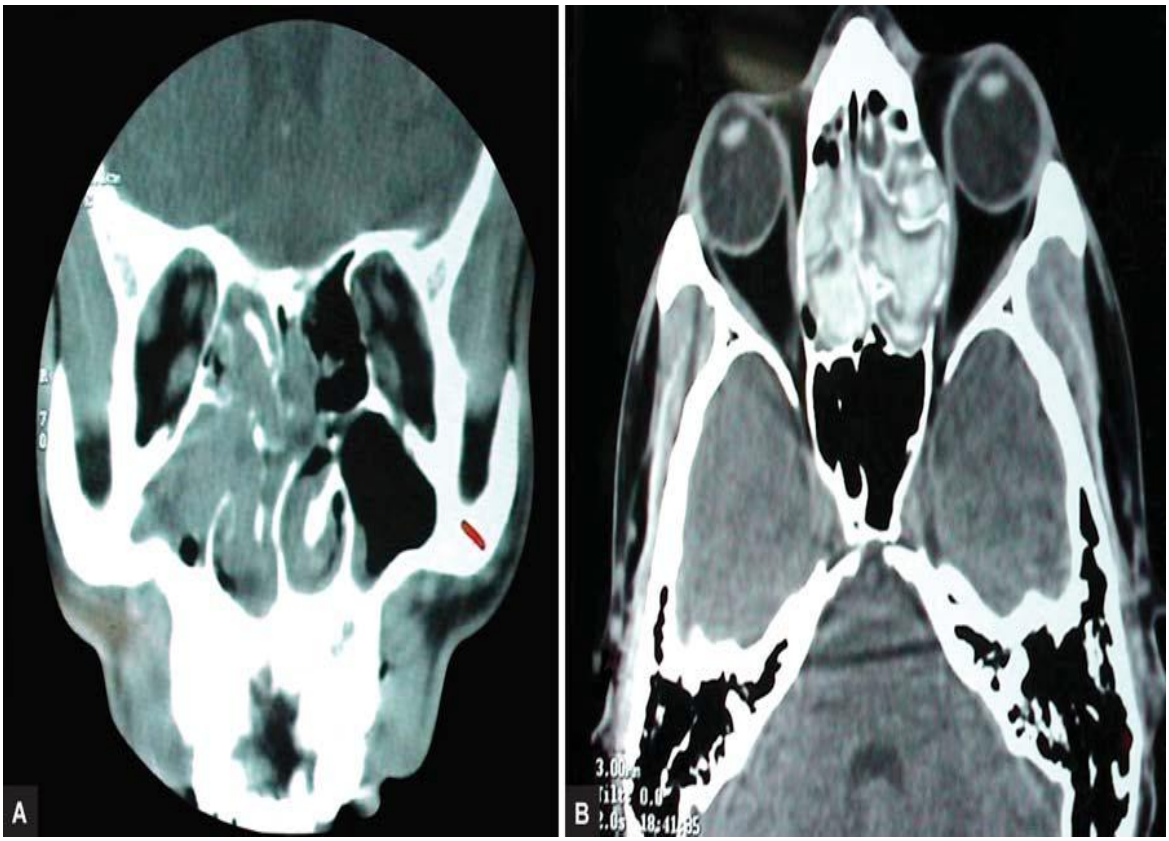
Axial CT – PNS showing expansion of the right sinonasal compartment with corresponding compromise of the right orbital volume, with remodeling of the right lamina papyracea, as compared to the left side, in a case with right sided AFRS.



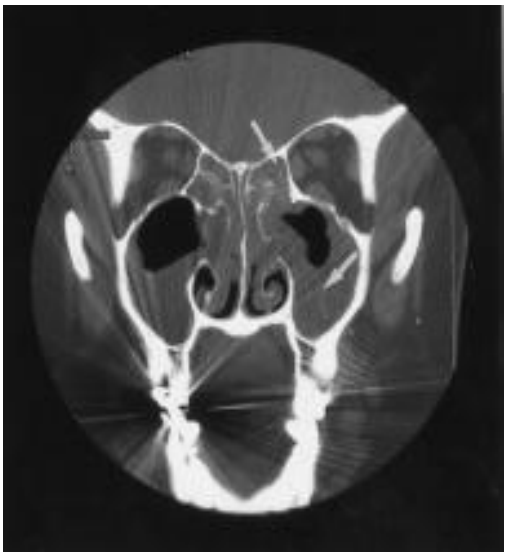
Axial CT – PNS showing the characteristic 'double density' sign, in a patient with right sided AFRS

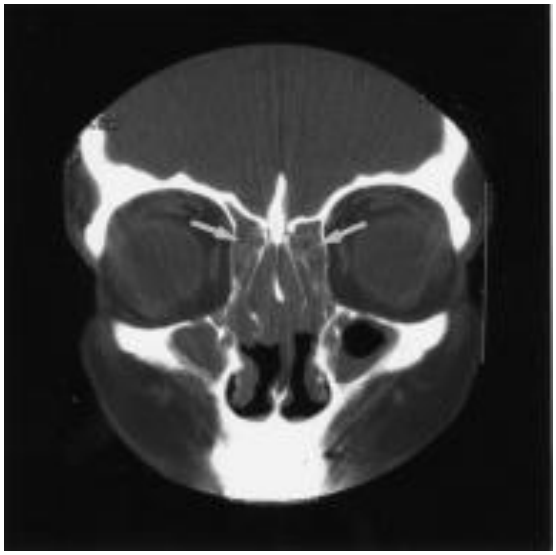


Preoperative, pre steroid axial CT – PNS showing a complete 'white-out' appearance, with involvement of both sides sinonasal compartments.

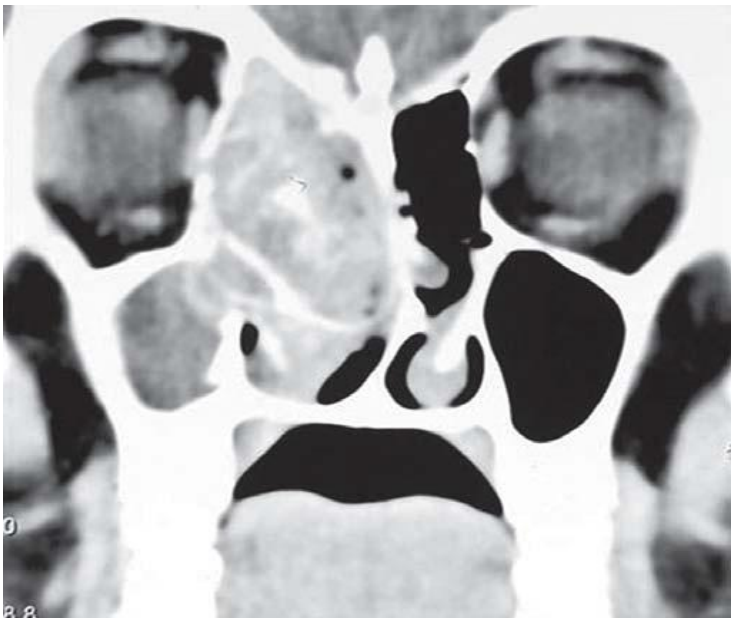


Computed tomographic findings in fungal sinusitis may include mucosal thickening, air fluid levels, osteomeatal complex obstruction and heterogeneous opacification with local areas of high signal densities due to heavy metal deposition within the sinuses.

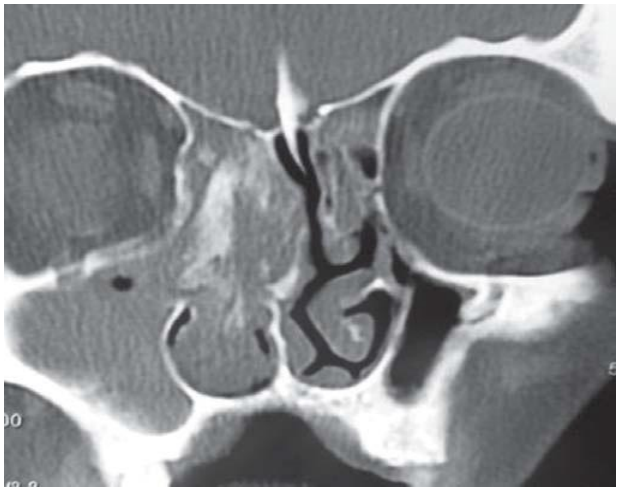




Coronal cuts of CT PNS showing inflammatory thickening of mucosa of involved sinus with areas of hyper attenuation.



Coronal CT – PNS showing unilateral (right sided) sinus opacification with hyper attenuation in a case of Allergic fungal rhinosinusitis (AFRS).

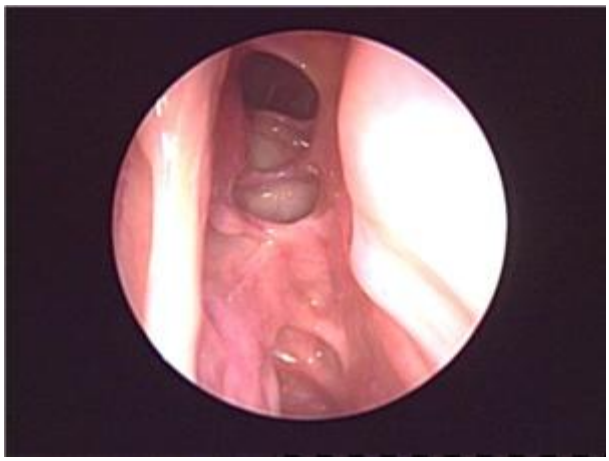


Coronal CT – PNS of a patient with AFRS showing extensive sinus involvement on the right side, with minimal disease on the left side.

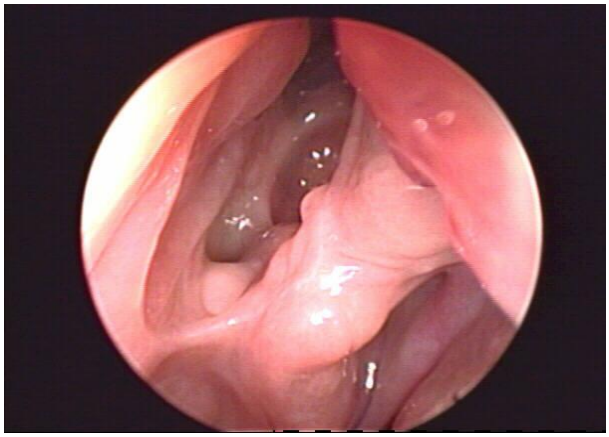
Endoscopic Mucosal Staging – in Allergic fungal sinusitis

STAGE	ENDOSCOPIC FINDING
0	No mucosal edema or allergic mucin
I	Mucosal edema with or without allergic mucin
II	Polypoid edema with or without allergic mucin
III	Sinus polyps with fungal debris or allergic mucin

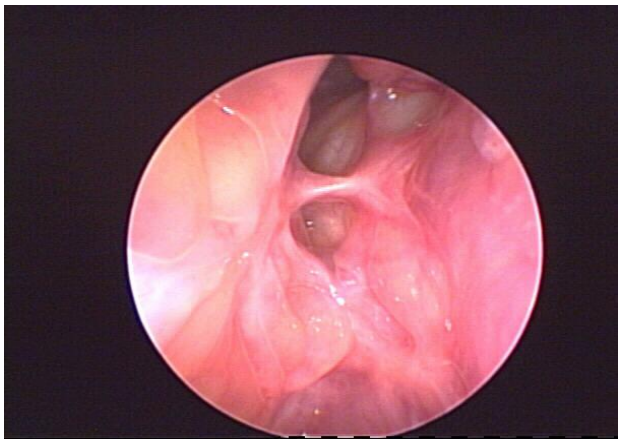
Kupferberg et al refined endoscopic follow-up into a staging system, for control of the nasal mucosal response to medical treatment , that is , oral steroids.



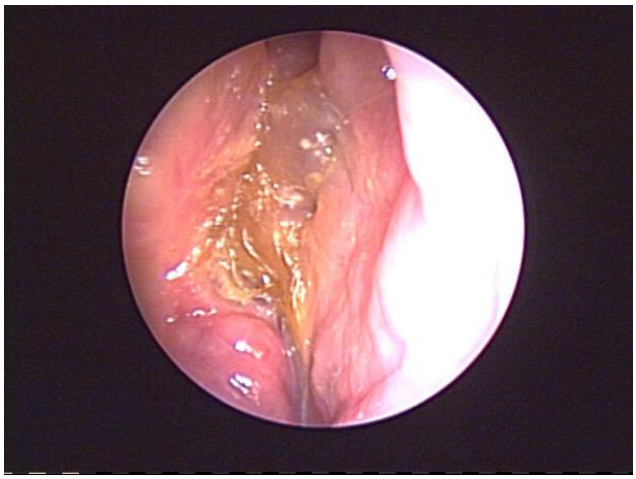
STAGE 0



STAGE 1



STAGE 2



STAGE 3

IgE levels:

Total serum IgE level generally are raised in Allergic Fungal Sinusitis (90%)**.**

Previously serum IgE level has been used as a parameter for the clinical activity of ABPA. So for the clinical activity of Allergic Fungal Rhinosinusitis, IgE levels have been used.

2. Eosinophilic Fungal Rhino Sinusitis:

In 1999, Ponikau et al showed the presence of fungal elements in 96% of patient's nasal mucus and < 25% of patient showed type 1 hypersensitivity. They found that presence of fungal elements along with eosinophils, charcot-Leyden crystals in their mucus. This showed that some variety of fungal elements stimulate eosinophils without IgE mediated reaction. This concept described in patients with Chronic Rhino Sinusitis show exaggerated humoral and cellular responses.

3. Eosinophilic Mucin Rhinosinusitis:

Ferguson described the presence of eosinophilic mucin without the presence of fungi in a proportion of Rhino sinusitis patients at her centre & named it as Eosinophilic Mucin Rhino Sinusitis.

It is a systemic disease of immunological dysfunction. This is characterized by aspirin hypersensitivity, asthma and bilaterality in nature. Thus oral corticosteroid is a useful drug in these individuals.

SURGICAL MANAGEMENT:

Once the diagnosis was confirmed, consent was obtained, surgery was planned. All noninvasive cases of fungal sinusitis have been operated on through an endoscopic endonasal approach.

FUNGAL BALL:

The technique includes wide opening of the diseased sinus cavity with removal of fungal ball. The mucous membrane was conserved, only a mucosal biopsy was made to eliminate fungal invasion if suspected. The procedure can be performed under local or general anaesthesia according to the extension of the fungus ball, favorable anatomic condition & patient's willingness.

ALLERGIC FUNGAL RHINOSINUSITIS & EOSINOPHILIC MUCIN SINUSITIS:

The surgical treatment of AFRS & eosinophilic mucin sinusitis is aimed at complete removal of the fungal antigenic material by completely removing the allergic mucin & debris from the sinuses, while simultaneously treating the underlying inflammatory process with

Medical management (systemic & topic corticosteroids).

Surgery should achieve permanent drainage & ventilation of the diseased sinuses, while simultaneously preserving the integrity of the underlying mucosa, once adequate drainage & ventilation of the sinuses is achieved, the diseased mucosa soon revert back to normal. Final goal is to achieve postoperative access to previously diseased areas.

ACUTE INVASIVE FUNGAL SINUSITIS:

Surgical treatment in Acute Invasive Fungal Sinusitis should be performed on an urgent basis as soon as the diagnosis is confirmed. Surgical debridement of all infected tissue within the nose & PNS by the endoscopic approach. The external approach may be inevitable when there is extensive disease of the lateral nasal wall or evidence of orbital, facial or intracranial extension. External procedures include any of the following; Medial maxillectomy, Total Maxillectomy with or without Orbital exenteration or Craniofacial resection.

Another important step in managing is administration of Amphotericin B. Rapid infusion of effective close should be undertaken. A test dose must be administered first with careful monitoring to avoid anaphylaxis. Usual dose is 1-3 hours daily, then advanced to 0.5mg or 0.6mg/kg/day or as toxicity permits.

Because the agent is fungi static rather than fungicidal, long term

(weeks – months) treatment is necessary with a cumulative dose of 2500 to 4000mg.

CHRONIC INVASIVE & CHRONIC GRANULOMATOUS FUNGAL SINUSITIS:

Surgical debridement of necrotic tissue until normal tissue is achieved is the ideal management for this condition. Endoscopic & external approaches can be considered in these cases.

IMMUNOTHERAPY:

The main concept of use of immunotherapy is to reduce the amount of crusting & polyposis & decrease the need for use of systemic & topical steroids. The basic protocol includes an initial test for allergy which may be done before/after surgery. The therapy has been started 4 to 6 weeks after surgery, in recurrent cases, revision surgery should be done before starting the immunotherapy. The patient is tested for fungal as well as non fungal antigens & all the positive reactors are prepared in 2 separate vials. Weekly injections are given from each vial in separate arms, with gradual stepping up of doses till the maximum tolerated dose is reached. This is to be continued for a year after which the dose has to be tapered over the next 2 years.

POSTOPERATIVE CARE:

Immediately in the post-operative period nasal saline irrigation should be followed .Weekly visits are required initially to allow regular inspection of the operative areas as well as debridement of crusts & retained fungal debris if necessary. Systemic corticosteroids are continued postoperatively at an individualized dosage based upon the overall plan of treatment.

FOLLOW UP:

Fungal Ball:

Long term follow up is usually not required once the disease is removed & patency of sinuses is maintained.

Allergic Fungal Rhino Sinusitis:

Long term follow up is required for maintenance of sinus cavities. This can be achieved via endoscopic examination. A short dose of steroids can be administered if any signs of recurrence are seen.

Acute Invasive Fungal Sinusitis:

This condition is usually associated with high mortality rate. Survivors may need long term follow up by several specialists.

Chronic Invasive Fungal Sinusitis:

This condition has tendency to recur & require long term follow up.

Chronic Granulomatous Fungal Sinusitis:

Prognosis is good, but tendency to recur exists.

MEDICAL MANAGEMENT:

Fungal Ball:

Surgical removal of fungal ball & ventilating the closed sinuses is the treatment of choice. No further medical treatment is indicated. Anti-fungal is not required.

Allergic Fungal Rhino Sinusitis:

Antibiotics are administered in the perioperative period.

Systemic steroids are started 7 days prior to surgery. Steroids are administered 1week preoperatively & atleast 4-6weeks postoperatively;

-to shrink the polyps

-to reduce mucosal inflammation

- to decrease the blood loss

Kuhn & Janer recommendation is to begin Oral Prednisolone in a dose of 0.4mg/kg per day (upto a maximum of 40mg) for 4 days. The

dose is reduced by 0.1mg/kg/day in cycles of 4 days until a dose of 20mg/day, or 0.2mg/kg/day, whichever is greater is reached. This is continued until 1month postoperatively, when it is adjusted to 0.2mg/kg/day. This dose is maintained & the patient is followed monthly with both nasal endoscopy & total serum IgE levels.

ANTI FUNGAL AGENT FOR TREATMENT OF INVASIVE FUNGAL SINUSITIS:

Amphotericin B (a polyene macrolide) is the standard drug for most life-threatening systemic fungal infections. Its broad spectrum of activity, combined with the potential for fungicidal activity makes it a useful agent for the treatment of most severe invasive mycoses. Despite its clinical effectiveness, toxicities associated with Amphotericin B administration, including infusion related reactions, electrolyte wasting & nephrotoxicity, have made its use problematic with many patients, particularly those with concomitant renal dysfunction or those receiving other nephrotoxic agents**.**

The administration of Amphotericin B , intravenous doses in the range of 0.25 to 1.0 mg/kg once daily (most commonly 0.4 to 0.7mg/kg/d) in 5% Dextrose solutions usually are recommended . Maximum daily doses of 1.2mg/kg/d in adults and 1.5mg/kg/d in children generally are reserved for serious invasive mycoses. Because of concerns

regarding hypersensitivity reactions, the product information recommends that a test dose (1 mg in 50 ml of 5 % Dextrose over 20 minutes) to be given before the administration of the first full dose of Amphotericin B.

AZOLES: IMIDAZOLES & TRIAZOLES:

These drugs offer antifungal activity against many fungal pathogen without the serious nephrotoxic effects observed with amphotericin B administration and have been shown to be effective in treatment of systemic mycoses. It has best activity against fungi such as Aspergillus & black moulds that typically cause fungal sinusitis & probably is the drug of choice for this site of infection unless there is extensive fungal invasion into bone, in which case initial therapy with amphotericin B may be necessary.

6. STUDY REVIEWS

1. Fabio Pagella, Elina Matfi, Paolo Casteinuova- To report the polilinico S.Matteo, University of Pavia experience, 81 patients presenting paranasal sinus fungal ball have been treated (Jan 1994 to May 2005). 27 men & 54 women (mean age-49.4yrs) were considered. 73 patients had a single sinus affected, but 8 presented multiple localizations. Maxillary was the most involved sinus followed by sphenoidal & ethmoidal. Histology showed fungal colonization but not invasion in all cases. Tomography showed bone erosion in 33.3% of patients. All have been treated only by FESS, of which 77 of 81 patients have been cured & remaining 4 needed another surgical management. Follow up was between 6 & 132 months (average 63 months).
2. Xavier Dufour, Catherine Kauffmann – Lacrox, Jean-Caide Ferie, Alexander karkas – They studied retrospective analysis of the results of FESS performed in 175 patients suffering from paranasal sinus fungal balls. All maxillary (150), sphenoidal (20) & ethmoidal (4) locations have been treated exclusively by FESS to obtain a wide opening of the affected sinuses, allowing a careful extraction of all fungal materials without removal of the inflamed mucous membrane. No major complications occurred.

Postoperative care was reduced to nasal lavage with topical steroids for 3 to 6 weeks. Only 1 case of local failure have been observed maxillary sinus(n =1) & 6 cases of persisting of fungal ball maxillary sinus(n=4), frontal sinus(n=2) with a mean follow up of 5 yrs. No medical treatment was required.

3. Klossek et al – 1997. They have showed in fungal ball cases, average age reported ranging from 28-86 years (no paediatric cases reported), 52% of patient had a normal preoperative endoscopy. Purulent nasal discharge is seen in about 38% of cases. As in any cases of chronic sinusitis a careful examination with rigid telescope is mandatory as the mucosal changes may be subtle & localized nasal polyps in the vicinity of the natural ostium of the involved sinus, which likely only represent an advance stage of nasal inflammation. Cultures for fungus was positive in only 30% of cases.
4. Mayo clinic, September 1999 – This prospective study evaluated the incidence of Allergic Fungal Sinusitis in 210 consecutive patients with Chronic Rhino Sinusitis with or without polyposis, of whom 101 were treated surgically. Fungal cultures of nasal secretions were positive in 202 of 210(96%) consecutive Chronic Rhino Sinusitis. Allergic mucin was found in 97 of 101(96%)

consecutive surgical cases of Chronic Rhino Sinusitis. Allergic Fungal Sinusitis was diagnosed in 94 of 101(93%) consecutive surgical cases with Chronic Rhino Sinusitis, based on histopathological findings & culture results. IgE mediated hypersensitivity to fungal allergens was not evident in the majority of Allergic Fungal Sinusitis patients.

5. Manning et al, 1996 - Of 263 cases of Allergic Fungal Sinusitis, 168 cases yielded positive fungal cultures. Of these positive cultures, 87% were from dematiaceous genera, while only 13% yielded Aspergillus.
6. John E Mcclay, the author & colleagues demonstrated a comparative study of AFRS between children and adult presentation which showed 88% versus 58% have asymmetric involvement. Unilateral disease was more common among children than adults in their study bilateral disease was more common among adults.
7. Schubert & Goetz reported the long term clinical outcome of 67 patients following initial surgical therapy for Allergic Fungal Sinusitis. Patients treated with at least 2 months of oral corticosteroids were compared to those who received no corticosteroids. At 1yr following initial surgery, patients with oral

corticosteroid were significantly less likely to have experienced recurrent Allergic Fungal Rhino Sinusitis (35%) than those who had not (55%).

8. Kathleen T. Montone, Virginia A. Livotsi, Michael D. Feldman, David W. Kennedy – A Retrospective review of Fungal Rhino Sinusitis of 400 patients at a single university medical center. 400 patients with Fungal Rhino Sinusitis were identified. 87.25% were non-invasive (45% Allergic Fungal Rhino Sinusitis; 40% Fungal Balls & 2% combined Allergic Fungal Rhino Sinusitis & 12.5% were Invasive Fungal Rhino Sinusitis, 11% Acute Fulminant Invasive Fungal Sinusitis, 1.2% Chronic Invasive Fungal Sinusitis, 0.5% Chronic Granulomatous Fungal Rhino Sinusitis & 0.25% had combined Fungal Ball/ Chronic Granulomatous Fungal Rhino Sinusitis. In their population, Invasive Fungal Rhino Sinusitis is rare with Acute Invasive Fungal Rhino Sinusitis representing >90% of cases. Culture data supports that a variety of fungal agents are responsible for Fungal Rhino Sinusitis but Aspergillus species appears to be one of the most common organism in patients with Fungal Rhino Sinusitis.

9. Blitzer et al, studied 179 cases of Acute Invasive Fungal Sinusitis having 70% prevalence of diabetes, 26% had other underlying diseases such as leukemia, renal disease, infant diarrhea, post-transplant immunosuppression, pancreatitis. Only 4% had no identifiable risk factors.
10. Blitzer & Lawson's study suggest the following common clinical signs of mucormycosis- cranial nerve deficit, proptosis, facial swelling, palatal ulcer, stupor & coma in the order of severity.
11. Blitzer & Ochi concluded that Acute Invasive Fungal Sinusitis needs surgery & systemic anti-fungal agents with radical debridement, the survival rate was 76% while the rate dropped to 57.5% with medical treatment alone. They could achieve 81% survival rate by combining Surgery & Amphotericin B therapy.
12. Rains et al (2003) have reported retrospectively that of the 139 patients of Allergic Fungal Rhino Sinusitis, treated with systemic corticosteroids & oral Itraconazole in the post-operative period, they found a reduced need for revision surgery.
13. Seiff et al (1999) have stated that more conservative surgical debridement with Amphotericin B irrigations is an adjunct in sino-orbital fungal infections, especially in patients with reversible immunosuppression & good preoperative visual activities.

14. Gillepsie & O'Malley in the author's series mucosal discoloration in acute fulminant invasive rhinosinusitis, middle turbinate (67% of patients) followed by septum (24%), palate (19%) & inferior turbinate (10%).

AIM OF THE STUDY

1. To Study the Epidemiology of Fungal Infections of Nose & Para Nasal Sinuses in our region.
2. To Study the Clinical Manifestation of Fungal Rhino Sinusitis.
3. To Study the Radiological & Pathological characteristics of Fungal Rhino Sinusitis.

METHODOLOGY

STUDY DESIGN – Prospective Study

STUDY PLACE – Department of ENT, Stanley Medical College Hospital

STUDY PERIOD – February 2011 to September 2012

SAMPLE – 30 Patients

INCLUSION CRITERIA:

- Both male & female sex
- Age groups 11-60 years
- All cases of Chronic Rhinosinusitis
- All cases of Nasal polyps with nasal discharge
- All cases of Rhinosinusitis with proptosis, headache & epistaxis
- Immunocompromised patients (Uncontrolled Diabetes Mellitus, Post transplant, HIV patients) who presented with features suspicious of fungal sinusitis.

- Patients with Fungal Rhinosinusitis were diagnosed by screening the patients with chronic Rhinosinusitis with or without nasal polyps.

EXCLUSION CRITERIA

- Patients with proven bacterial sinusitis
- Patients with associated neoplastic lesion were excluded
- Medically & surgically unfit patients.
- Not willing for study
- Bleeding diathesis

CLINICAL DIAGNOSIS OF RHINOSINUSITIS

It is based on Major & Minor Criteria described by Lanza & Kennedy.

MAJOR	MINOR
Facial pain or Facial Pressure	Headache
Facial congestion or Facial Fullness	Halitosis
Nasal block or nasal discharge or Post nasal drip	Fatigue
	Dental pain
Hyposmia orAnosmia	Cough
Purulent secretions in nasal cavity on anterior Rhinoscopic examination	
Fever (Acute Rhinosinusitis)	

DIAGNOSTIC CRITERIA FOR ACUTE FUNGAL RHINO SINUSITIS

Bent & Kuhn diagnostic criteria for AFRS

I	II
Type I Hypersensitivity	Asthma
Nasal Polyposis	Unilateral predominance
Characteristic CT findings	Radiographic bone erosion
Positive Fungal stain or culture	Fungal culture of mucin
Allergic mucin with fungal hyphae without tissue invasion	Charcot-Leyden crystals
	Serum eosinophilia

All selected patients were made familiar with the study plan. Detailed History taking, Clinical examinations & complete examination of Ear, Nose & Throat was done.

A total of 30 patients whose clinical picture suggests Chronic Rhinosinusitis & gives suspicion of Fungal Rhinosinusitis were subjected

to detailed history taking & clinical examinations, underwent the following investigative procedures methodically.

A) HAEMATOLOGICAL INVESTIGATIONS:

Complete Hemogram, Blood Sugar level, Serum Electrolytes, Serum Proteins, Blood Grouping, etc. HIV/HBsAg was done to assess the general condition of the patient.

B) DIAGNOSTIC NASAL ENDOSCOPY

C) RADIOLOGICAL PROCEDURES:

Relevant X Rays of the nose & paranasal sinuses were taken for those who were provisionally diagnosed as fungal Rhinosinusitis were subjected to CT of nose, Paranasal sinuses.

ENT examination:

A thorough history of nasal block, facial pain, nasal discharge, headache, hyposmia, fever of unknown origin after 48hours of appropriate Broad spectrum Antibiotics.

Anterior & posterior rhinoscopy examination was done to look for any anatomical variation that may predispose to fungal infections of nose and paranasal sinus and to assess any pathological lesion in nose.

X ray PNS (Water's view) & additional views if needed were done.

A thorough Rigid endoscopic nasal examination was done under

local anaesthesia.

CT PNS axial & coronal cuts of 2mm slice were ordered in those patients who were found to have evidence of pathology.

A complete examination of Head & Neck region was performed on all selected patients in addition to the Endoscopic examination of nose. The mental status of patients provides a rough evaluation of CNS function. All cranial nerve examination with particular attention to sensation of face, ocular movements, afferent pupillary reflex and visual acuity were performed in those cases suspected of Invasive Fungal Rhino sinusitis. The eyes were assessed of conjunctival irritation or tearing.

Examination of oral cavity & oropharynx was done to note the presence of any palatal defects or postnasal discharge.

The underlying causes of Immunodeficiency were evaluated. Total serum IgE level & Total Eosinophil count were taken. Microscopic evaluation of mucin along with fungal culture was evaluated intraoperatively in those cases of suspected AFRS.

Biopsied specimen were placed in 3 sterile bottles-

Bottle A - Specimen with Normal saline

Bottle B - Specimen with Normal saline

Bottle C - Specimen with diluted Formalin solution.

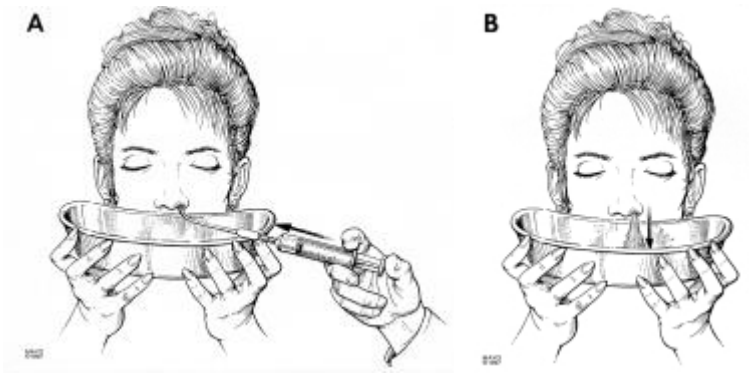
Bottle A & B were sent to Microbiological lab within one hour of

the procedure.

The ideal technique for use in mycology & bacteriology laboratories is the KOH- Calcofluor white method. The technique uses KOH to dissolve human material & an optical brightener called calcofluor white that binds to the cell wall of the hyphae. Fungal cell walls, including septations, fluorescence, intensely when viewed using fluorescence microscopic equipped with correct filters.

Bottle C was used for histopathological examination of the specimen under low & high power magnification with a light microscope.

COLLECTION OF MUCUS:



-*Saline is instilled forcefully into the patient's nostril.*

The patient exhales saline & mucus into a sterile pan.

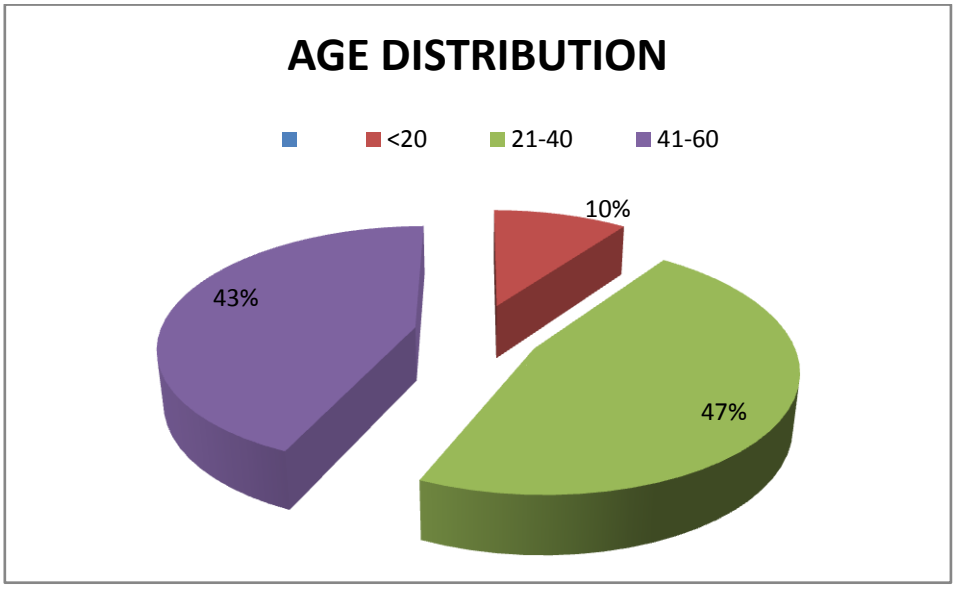
Based on the concept that fungi colonize the mucus make the development of a simple non-invasive procedure to obtain mucus as much as possible for examination. 2 puffs of phenylephrine (1%) are

sprayed into each nostril to produce vasoconstriction. After 2 minutes each nostril is flushed with 20ml of sterile saline. The return is collected in a sterile pan. The collected fluid is allowed to centrifuge & sent to the mycology laboratory.

RESULTS

AGE DISTRIBUTION:

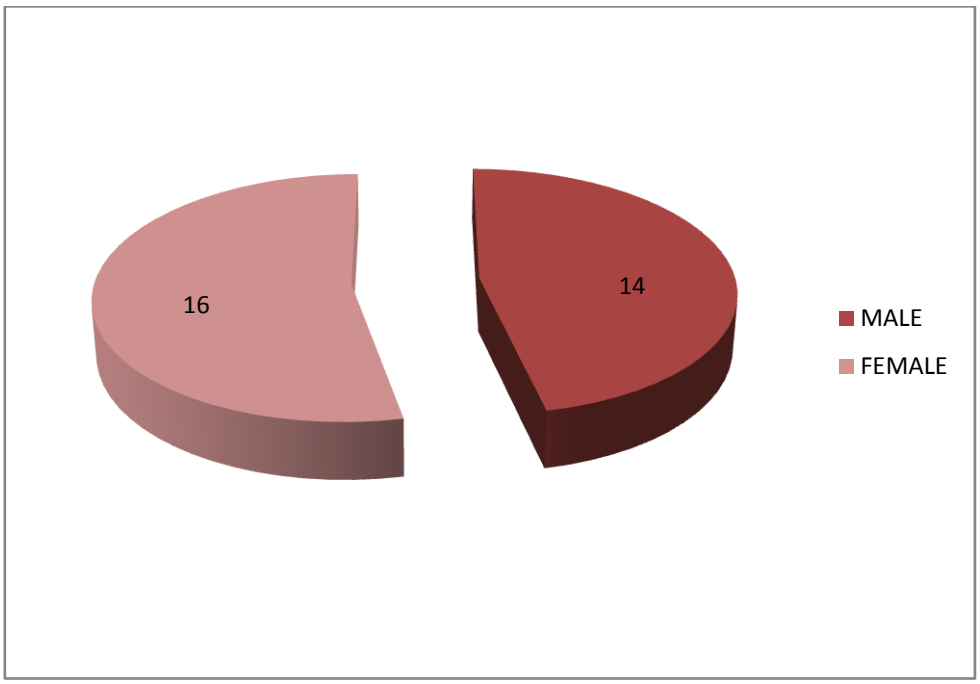
AGE	NO OF PATIENTS	PERCENTAGE%
<20	3	10%
21-40	14	46.6%
41-60	13	43.3%



Most cases of Fungal Rhino sinusitis in the study were in the Age group between 21-40 years.

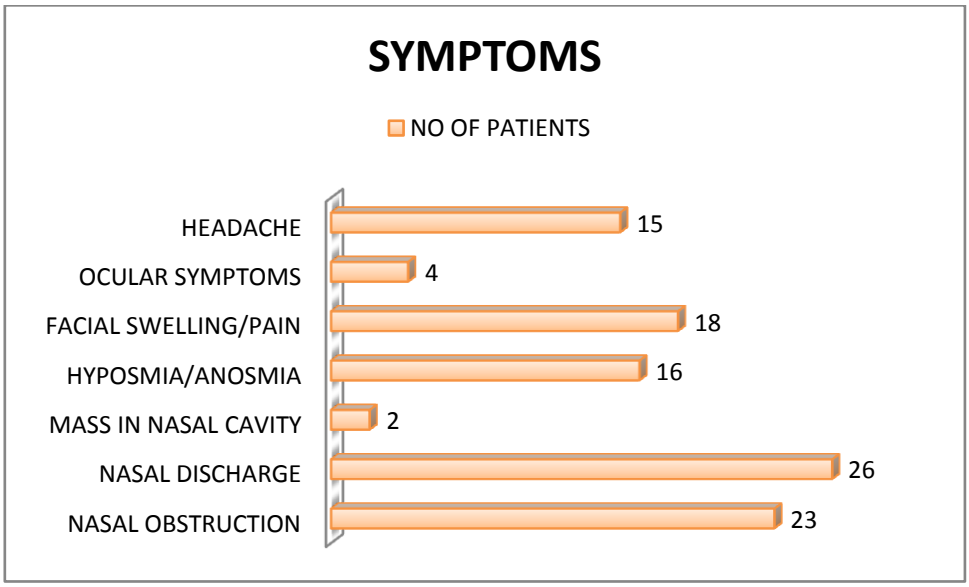
SEX DISTRIBUTION:

TOTAL CASES	MALE	FEMALE
30	14	16



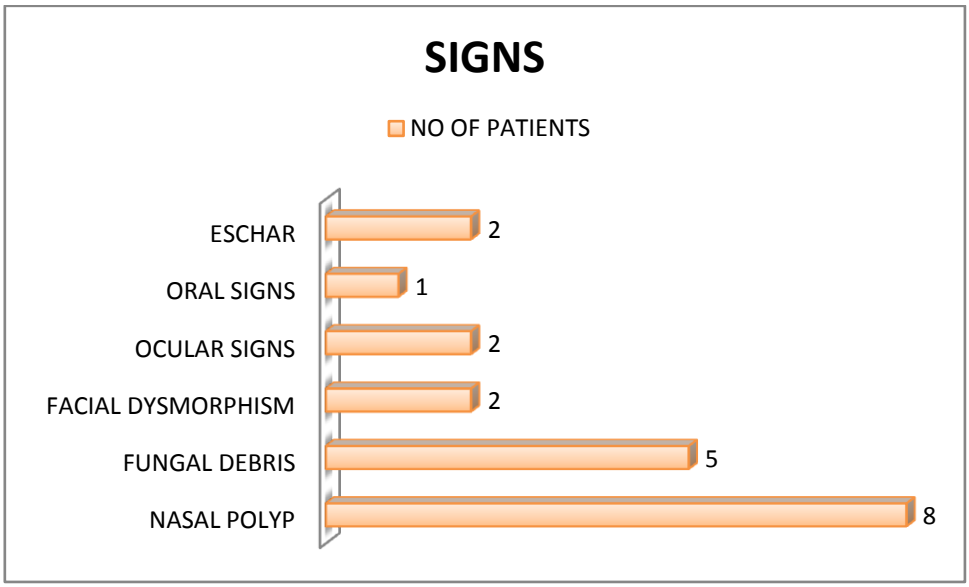
The above observation suggests almost equal incidence of Fungal sinusitis among both the sex.

SYMPTOMS:



All the patients in the study have Nasal symptoms such as nasal block, nasal discharge, hyposmia or anosmia, facial swelling or facial pain. 2 patients presented with mass in nasal cavity. Out of 30 patients, 15 patients had headache (50%) and only 4 patients presented with ocular symptoms such as watering eyes, blurring of vision.

SIGNS:



In the current study, Anterior Rhinoscopic examination of the nose showed Nasal polyp in 8 patients, Fungal debris in 5 patients.

Only 2 patients presented with Facial Dysmorphism

(i.e) widening of nasal bridge

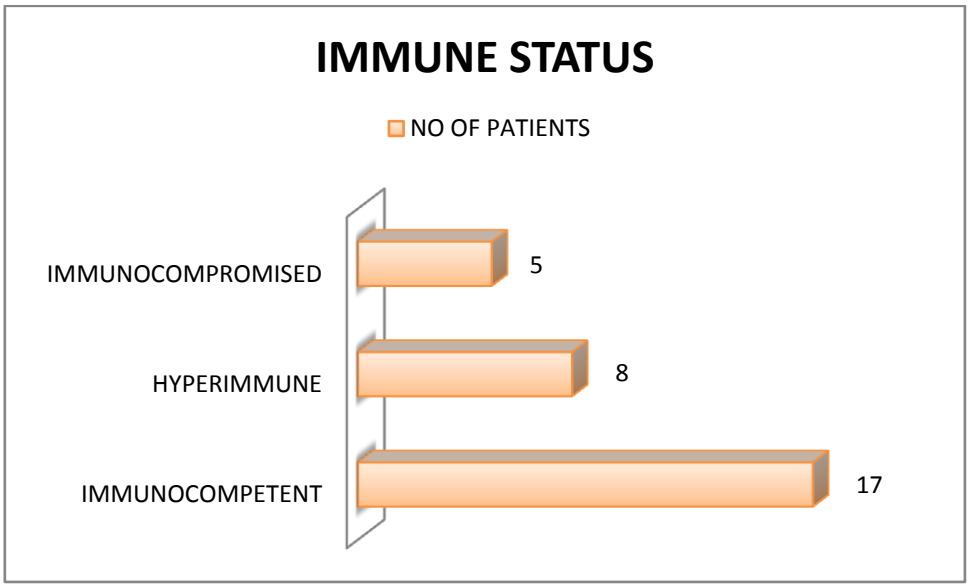
Only 2 patients presented with ocular signs such as Proptosis, periorbital swelling, watering of eyes, and loss of vision. Only 1 patient had blackish discoloration of mucosa over hard palate.

2 patients had eschar .

6 patients presented with ocular signs such as ophthalmoplegia proptosis & loss of vision.

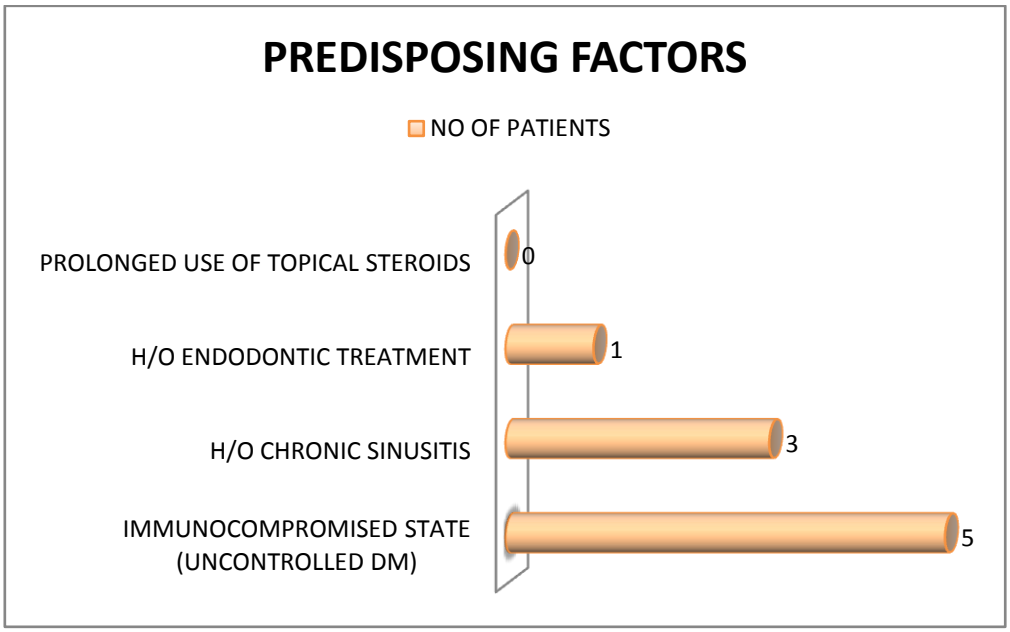
Only 1 patient had oral sign – fistula in hard palate with blackish discoloration of oral mucosa.

IMMUNE STATUS:



Out of 30 patients, 17 were Immunocompetent, 8 were Immunologically Hyper competent and 5 were Immunocompromised. The Immunocompromised state that was observed in the current study was Diabetes Mellitus(100%)

PREDISPOSING FACTORS:



The various predisposing factors for fungal sinusitis encountered in the current study were

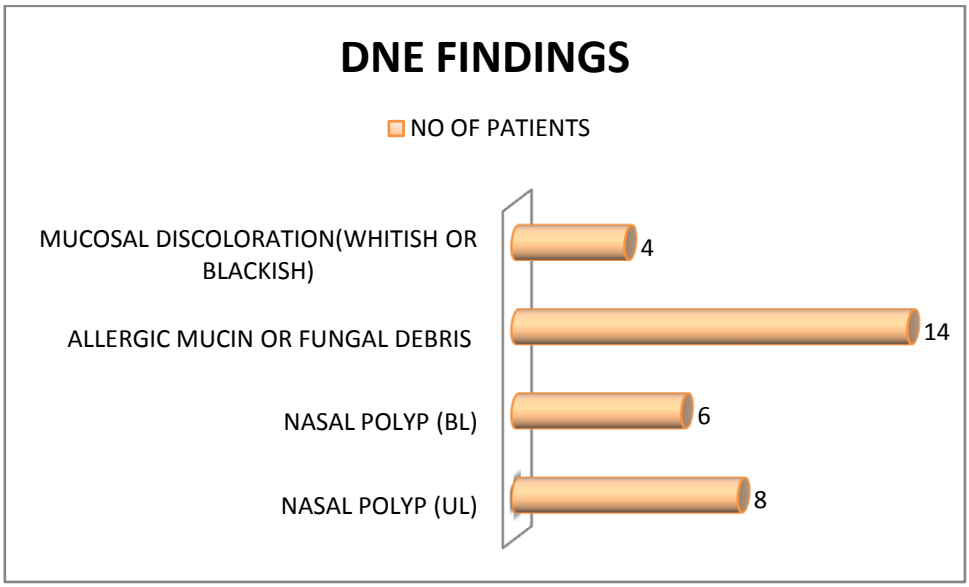
a) History of chronic sinusitis (n=3)

b) Previous h/o endodontic treatment (n=1)

c) Immunocompromised conditions(n=5)

d) None of patients had history of prolonged usage of steroid, antibiotics.

DIAGNOSTIC NASAL ENDOSCOPY FINDINGS:



Out of 30 patients in the current study, 22 patients had associated Deviated Nasal Septum, of which 5 patients had Turbinoseptal-3 type of Deviated Nasal Septum which may be the possible risk factor for Osteomeatal complex block → Poor sinus ventilation → Stasis of secretions → Inhaled fungus proliferation & antigenic exposure.

14 patients had nasal polyps, of which 8 had unilateral side and 6 had bilateral nasal polyps. These patients also had allergic mucin, so evaluated for Allergic Fungal Rhinosinusitis and diagnosed as AFRS.

4 patients had nasal mucosal discoloration which may be whitish or blackish discoloration in areas such as middle turbinate, septum, lateral nasal wall noted in patients of Acute Fulminant Invasive Fungal sinusitis.5 patients had mucosal discoloration in areas such as middle

turbinate, septum, inferior turbinate and lateral nasal wall which were diagnosed as Acute Invasive Fungal Rhinosinusitis.

CATEGORIZATION OF FUNGAL RHINO SINUSITIS:

DIAGNOSIS	NO OF CASES	M:F	AVERAGE AGE	CULTURE +VE CASES	COMMON ORGANISMS ISOLATED
FUNGAL BALL	11	4:7	38	3	ASPERGILLUS
AFRS	14	9:5	37	3	ASPERGILLUS
AIFRS	5	1:4	50	5	RHIZOPUS
CIFRS	0	-	-	-	-
CGFRS	0	-	-	-	-

(AFRS - Allergic Fungal Rhino sinusitis, AIFRS - Acute Invasive Fungal Rhino sinusitis, CIFRS - Chronic Invasive Fungal Rhino sinusitis, CGFRS - Chronic Granulomatous Fungal Rhinosinusitis)

Out of 30 cases, 11 cases were fungal ball, 14 were Allergic Fungal Rhinosinusitis and 5 were Acute Fulminant Invasive Fungal Rhinosinusitis. There were no cases of Chronic Invasive Fungal Rhinosinusitis observed in our study.

CLINICAL MANIFESTATION OF FUNGAL BALL:

Out of 30 patients in the current study, 11 patients were diagnosed as Fungal ball.

1. All patients presented with symptoms such as Nasal obstruction, Facial pain, Head heaviness, Hyposmia

2. All these patients had no Allergic symptoms.

3. None of these patients had polyps.

4. 1 patient had History of Endodontic treatment.

CLINICAL MANIFESTATION OF ALLERGIC FUNGAL RHINOSINUSITIS:

Out of 30 patients in our study group,14 patients were diagnosed as Allergic Fungal Rhinosinusitis.

1. Most of these patients presented with symptoms of allergy such as sneezing, watery rhinorrhea, expelling dark coloured rubbery nasal discharge, headache.

2. 2 patients presented with mass in nasal cavity.

3. 1 patient presented with proptosis along with other nasal symptoms

On examination all 14 patients had nasal polyps of which 8 were Unilateral & the rest 6 were Bilateral.

CLINICAL MANIFESTATION OF ACUTE FULMINANT INVASIVE FUNGAL RHINOSINUSITIS:

In our study of 30 patients with Fungal Rhinosinusitis, 5 patients were diagnosed as Acute Fulminant Invasive Rhinosinusitis.

1. All 5 patients were in the immunocompromised state of Type II Diabetes Mellitus. Their blood sugar levels were fluctuant in nature.

2. 2 patients had urine ketone positive.

3. 1 patient presented with headache, periorbital pain, nasal congestion, rhinorrhea. Imaging studies was taken for the patient and was diagnosed as disease in maxillary, anterior and posterior ethmoid sinuses. Hence the patient underwent Endoscopic Sinus Surgery → Wide Middle Meatal Antrostomy & Complete Ethmoidectomy was done. Histopathological examination of specimen showed hyphal form within the submucosa without angioinvasion, minimal host inflammatory cell infiltration suggestive of mucormycosis. Fungal culture positive for rhizopus.

4. Second patient presented with facial necrosis, facial deficit, bare bone exposure with eschar . Radical surgical debridement was done for that case and histologically proven as mucormycosis.

5. Other 2 patients presented with fever, headache, eschar over the middle turbinate & septum. Of which one had blackish discoloration of

mucosa over left side of hard palate. Surgical debridement was done for these patients and proven as mucormycosis.

6. One patient admitted at Intensive Medical Care Unit with altered sensorium, he had nasal congestion, purulent nasal discharge, fever, periorbital edema with eschar. Imaging studies such as CT PNS and MRI Brain has taken for this patient. Histopathological examination showed bony necrosis, septate hyphae consistent with Aspergillus sp. and inflammatory cell infiltrate, and tissue necrosis.

FUNGAL CULTURE RESULT IN 11 FUNGAL BALL CASES:

SINGLE FUNGAL ISOLATE	CULTURE RESULT	NO OF CASES
ASPERGILLUS SP.	A.fumigates	2
	A.flavus	1
	A.terreus	0
	A.niger	0
DEMATIACEOUS SP.	ALTERNARIA/BIPOLARIS/CURVILARIA	0
OTHERS		0

In the study, Aspergillus species was the common fungus isolated in the culture of Fungal ball cases.

CLINICAL SUMMARY OF AFRS:

AGE RANGE	SEX M:F	POLYPS	ATOPY	ASTHMA	HYPHAE IN HISTOPATHOLOGY	FUNGAL CULTURE	ELEVATED IgE
14-55	9:5	14	8	3	8	3	14

14 AFRS cases in our study, all patients had nasal polyps(100%)out of which, 8 unilateral nasal polyps and 6 bilateral nasal polyps. In 14 cases, 3 patients had asthma. Histopathology of allergic mucin in these patients showed, Eosinophils, Charcot Leyden crystals and sparse hyphae in 8 patients. 3 patients showed positive fungal culture. There were positive for Aspergillus species.

HISTOPATHOLOGICAL RESULT IN 14 ALLERGIC FUNGAL RHINO SINUSITIS CASES:

TOTAL NO OF AFRS PATIENTS	14
HISTOPATHOLOGICAL POSITIVITY	8

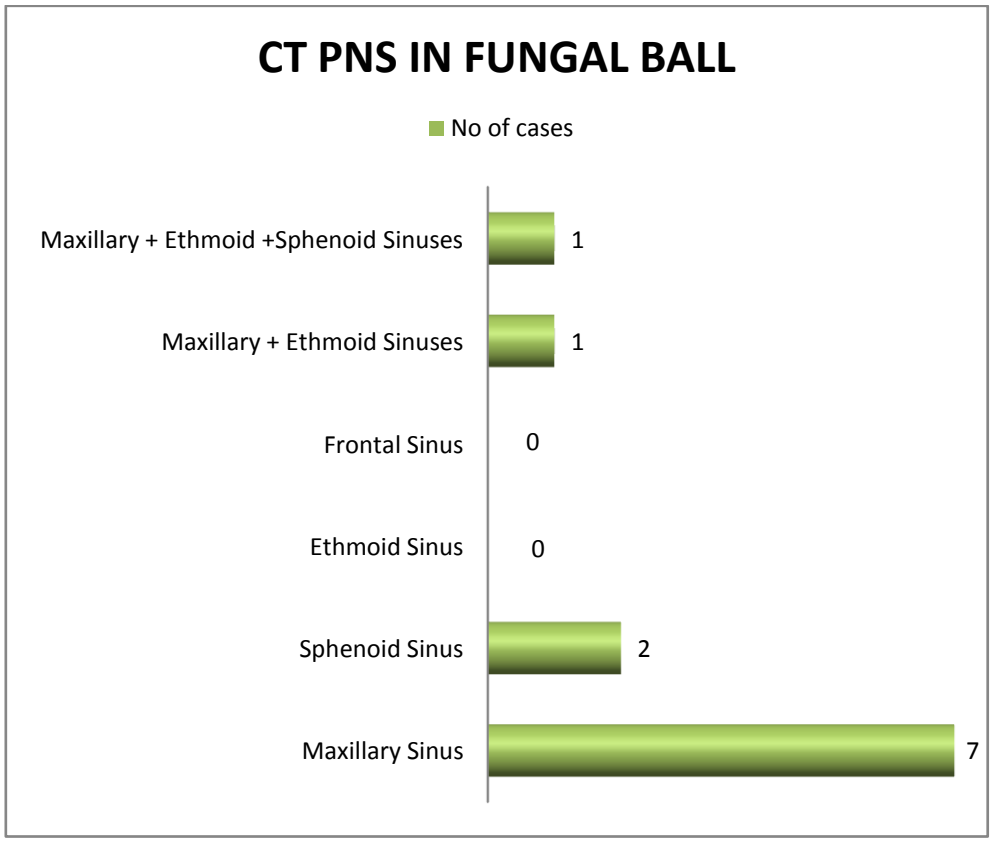
Histopathological Examination of allergic mucin with Hematoxylin and Eosin stain in Allergic Fungal Rhinosinusitis cases showed eosinophils, charcot – leyden crystals and fungal hyphae in 8 patients.

FUNGAL CULTURE RESULT IN 5 ACUTE INVASIVE FUNGAL RHINO SINUSITIS CASES:

SINGLE FUNGAL ISOLATE	NO OF CASES
ASPERGILLUS SP.	1
RHIZOPUS SP.	4

In the study, most of Acute Invasive Fungal Sinusitis showed Rhizopus sp. (80%) in fungal culture.

CT PNS IN FUNGAL BALL:



In the current study, coronal section of PNS in 11 Fungal Ball cases showed complete or subtotal opacification of maxillary sinus in 7 cases, sphenoid sinus in 2 cases, maxillary and ethmoid sinuses , maxillary, ethmoid and sphenoid sinuses in 1 case each.

Characteristic CT findings noted in Allergic Fungal Rhinosinusitis cases were central areas of hyper attenuation within the involved sinus cavity.

DISCUSSION

DIAGNOSIS	HANUMANTHUS ET AL	INTERNATIONAL JOURNAL OTOLARYNGOLOGY 2012	CURRENT STUDY
FUNGAL BALL	1.60%	40.25%	**36.67%**
AFRS	23.80%	45.00%	**46.67%**
AIFRS	28.50%	11.00%	**16.67%**
CIFRS	15.87%	1.00%	**0.00%**
CGIFRS	30.00%	0.50%	**0.00%**

The current prospective study on Fungal Rhino Sinusitis in our department which receives many referrals for surgical management of chronic sinusitis was done for 30 patients. Most of the patients, we observed come under the category of Non-Invasive form of Fungal Sinusitis with a distribution of Allergic Fungal Rhino Sinusitis(46.67%) and Fungal ball(36.67%) contributing to the majority of cases. On the whole, Invasive form was less (16.67%) with Acute invasive Entity predominating almost 100% of these cases (Chronic Invasive Fungal Rhino Sinusitis & Chronic Granulomatous Invasive Fungal Rhino Sinusitis = 0%).

Relatively similar distribution has been noted in other studies as shown in the table above.

DISCUSSION ABOUT FUNGAL BALL:

STUDY	NO OF CASES	FEMALE : MALE	AGE RANGE	FUNGAL CULTURE
DeShazo et al	**25**	**1.5:1**	**18-80**	**A.fumigatus (3) A.flavus (1) P.boydii (2) No growth (7)**
Ferreiro et al	**29**	**1.6:1**	**28-86**	**A.fumigatus (2) A.flavus (2) P.boydii (1) No growth (17)**
Klossek et al	**109**	**1.9:1**	**20-86**	**A.fumigatus (33) No growth (76)**
Current Study	**11**	**1.8:1**	**25-55**	**A.fumigatus (2) A.flavus (1) No growth (8)**

AGE - Average age in Ferreiro et al retrospective series of 29 cases was 65 years, ranging from 28 – 86 years. DeShazo and klossek et al showed a similar age range(20-80 years). No pediatric cases have been reported in the above studies which correlate with the current study. In the current study, the incidence of the fungal ball was in the age range of 25 – 55 years. The elderly age (>60 years) was not observed in the current study which could be attributed to the average age of an Indian (63years) & small sample size.

SEX - In the above studies, there is a considerable female predominance. In the current study the female to male ratio is 1.8:1 which

reconfirms the above finding. The exact reason remains unexplained. A possible reason is that, fungal ball are more common in older population, women outnumber men in the older population.

FUNGAL CULTURE - In the Ferrerio et al study, 17 out of 22 cases showed no growth (77%). In deShazo's literature review no fungal growth occurred 50% of the times ; however 11 cases were not cultured. Similarly in Klossek's review, 69% of cases had no growth. In current study, no growth was obtained in 8 cases (73%).

This difficulty in getting fungi to grow may be attributed to culture techniques (over homogenization of the specimen) or lack of viability of the fungi, which may be months old.

Common fungi, reported to cause fungal balls in all the above reviews is Aspergillus sp. In current study, 3 fungal cultures showed Aspergillus sp.

LOCALIZATION OF FUNGAL BALL:

STUDY	NO OF CASES	MAXILLARY SINUS	SPHENOID SINUS	ETHMOID SINUS	FRONTAL SINUS	MULTIPLE SINUSES
deShazo	25	18	4	0	3	0
Ferreiro et al	29	20	10	8	4	12
Klossek et al	109	97	9	3	2	7
Current Study	11	7	2	0	0	2

From the above study reviews, Maxillary sinus is the commonly affected, followed by sphenoid, although multiple sinuses may be affected. In current study, the predominant sinus involved is the maxillary(63%), followed by the sphenoid sinus(18%) and the rest (18%) involving multiple sinuses.

DISCUSSION ABOUT ALLERGIC FUNGAL RHINO SINUSITIS:

STUDY	AGE RANGE	SEX	ATOPY	ASTHMA	POLYPS	HYPHAE IN HISTOLOGY	+ve FUNGAL CULTURE	ELEVATED IgE
deShazo	7 – 58	52% (M) 48% (F)	76.50%	56.30%	80.20%	80.90%	75.50%	74.30%
Current Study	14 – 55	64% (M) 36% (F)	57%	21%	100%	71%	21%	100%

In the current study Allergic Fungal Rhino Sinusitis was observed in 14 out 30 (46.67%) patients. The Age Range in the current study was 14-55 years which was comparable to the previous study by deShazo et al (7-58years).

The sex incidence showed a Male predominance (64%) comparable to previous studies. Manning Holman noted a male predominance of 1.6 males per female (61%)

The incidence of polyposis was 100% in the current study, i.e all the patients presented with polyps.

The incidence of Asthma in Allergic Fungal Rhino Sinusitis was 33% to 50% according to Houser & Corey. In the Current study the incidence was noted as 21%.

Allergic Fungal Rhino Sinusitis was confirmed based on the Histo pathological examination of allergic mucin containing fungal hyphae or allergic mucin without fungal hyphae but positive fungal

cultures. In the current study 14 patients with allergic mucin were identified, of which 8 had fungal elements present on Histopathological Examination. Of the remaining 6 patients without Histopathological fungus 3 had positive fungal cultures. The remaining 3 patients with allergic mucin either had negative cultures or unknown culture results were considered to have less evidence for a pathologic diagnosis of AFRS. Although since other techniques for fungal detection such as PCR were not performed in these patients, they still may actually have AFRS.

The most common isolate in fungal culture in Allergic Fungal Rhino Sinusitis patients in the current study were Aspergillus sp. Unlike our observation, other studies showed predominantly dematiaceous fungi in culture. In Granville et al study almost 70% of AFRS cases grew dematiaceous fungi in culture. Schubert and Goetz observed that more than 80% of AFRS cases were associated with dematiaceous fungi and only 9% were due to Aspergillus sp.

DISCUSSION ABOUT ACUTE INVASIVE FUNGAL SINUSITIS:

5 out of 30 patients (17%) were diagnosed as Acute Invasive Fungal Rhino Sinusitis in the Current study. The sex distribution was 1 male & 4 female. The predisposing factor in all these cases was Diabetes Mellitus. The physical findings in these patients were commonly the mucosal abnormalities, were noted predominantly in the middle turbinate (60%) & septum (40%) followed by palate (20%) which were comparable to the findings of Gillespie & O'Malley study.

MUCOSAL ABNORMALITIES	Gillespie & O'Malley study	CURRENT STUDY
MIDDLE TURBINATE	**67%**	60%
SEPTUM	**24%**	40%
PALATE	**19%**	20%
INFERIOR TURBINATE	**10%**	0%

Out of 5 cases, 4 cultures were positive for Rhizopus sp.(80%) of Mucoraceae family & 1culture was positive for Aspergillus sp.(20%). The incidence of predominance of Rhizopus sp. in the current study compared to predominance of Aspergillus sp. in the previous studies may be attributed to increased incidence of Rhizopus species in Diabetes Mellitus patients. Ferguson studied 126 patients of rhinocerebral mucormycosis, of which 70% were diabetic. Rhizopus organisms have an

active ketone reductase system & hence thrive in high glucose, acidotic conditions. Normal serum inhibits rhizopus growth, whereas serum from patients in Diabetic ketoacidosis stimulates growth.

FUNGAL CULTURE RESULT IN ACUTE INVASIVE FUNGAL SINUSITIS

FUNGAL CULTURE	INT JOURNAL OF OTOLARYNGOLOGY 2012	CURRENT STUDY
Aspergillus sp.	49%	20%
Rhizopus sp.	33%	80%
Fusarium sp.	6%	0%
Alternaria sp.	6%	0%
Paecilomyces sp.	6%	0%

CLINICAL SUMMARY OF FUNGAL RHINO SINUSITIS:

DIAGNOSIS	MALE : FEMALE		NO OF CASES		CULTURE (% POSITIVE)		COMMON ISOLATES (%)	
	INT JOURNAL OF OTOLARYNGOLOGY 2012	CURRENT STUDY	INT JOURNAL OF OTOLARYNGOLOGY 2012	CURRENT STUDY	INT JOURNAL OF OTOLARYNGOLOGY 2012	CURRENT STUDY	INT JOURNAL OF OTOLARYNGOLOGY 2012	CURRENT STUDY
FUNGAL BALL	1:2	1:1.8	161	11	51.00%	27%	Aspergillus sp. (66%)	Aspergillus sp.
AFRS	1.2:1	1.8:1	180	14	89.00%	21%	Dematiaceous fungi (36%) Aspergillus sp. (35%)	Aspergillus sp.
AIFRS	1.5:1	1:4	44	5	67.00%	100 %	Aspergillus sp. Rhizopus sp.	Rhizopus (4) Aspergillus sp. (1)
CIFRS	1:1	0	4	0	100.00%	0%	C.albicans Scedosporium	0
CGIFRS	1:1	0	2	0	100.00%	0%	A.flavus	0

CONCLUSION

In a Prospective study of 30 patients with Fungal Rhinosinusitis;

1. The most common age group with Fungal Rhinosinusitis was between 21-40 years of age.
2. Non-Invasive Fungal Rhinosinusitis (Fungal Ball & Allergic Fungal Rhinosinusitis) was more commonly encountered in our region.
3. Fungal Ball was most commonly caused by Aspergillus species involving especially the maxillary sinuses with reportedly equal incidence in both the sexes.
4. Allergic Fungal Rhinosinusitis was common among the male sex & all the patients presented with Nasal polyps & Allergic Mucins. Most of them showed Histopathological positivity in our study population.
5. Invasive type of Fungal Rhinosinusitis was less commonly reported, it was more commonly Acute in presentation.
6. Mucoracea family - Rhizopus appears to be the common isolate in Acute Invasive form of Fungal Rhinosinusitis.

7. The Acute Fulminant Invasive form presented with wide spectrum of manifestation from simple sinusitis form to extensive Facial Necrosis. In this study, it was common in the elderly population who were Immunologically compromised due to Diabetes Mellitus.

8. Chronic Invasive form of Fungal Rhinosinusitis was least/not reported in this study.

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PROFORMA

A STUDY OF FUNGAL DISEASES OF THE NOSE AND PARANASAL SINUSES

Name of the patient :

age :

Sex :

S.No :

Place of residence :

Occupation :

Socioeconomic Status :

Hospital Number :

HISTORY

A) COMPLAINTS DURATION

1)

2)

3)

B) H/O Present Illness

NOSE:

SYMPTOMS DURATION

I) Nasal obstruction R/L/B

II) Nasal Discharge R/L/B

III) Headache

IV) Facial pain Unilateral / Bilateral

V) Nasal Bleeding R/L/B

VI) Change of voice

VII) Smell disturbances Hyposmia / Anosmia

VIII) Nose deformity

EYE

I) Proptosis

II) Pain

III) Watery Eyes

IV) Blurring of vision

V) Diplopia

ORAL CAVITY

I) Pain

II) Palatal ulcer

III) Mouth ulcer

CRANIALNERVES:

I) Anosmia

II) Loss of vision

III) Diplopia

IV) Ophthalmoplegia

V) Trigeminal Anaesthesia

VI) Facial palsy

VII) Nasal regurgitation

MISCELLANEOUS:

H/O Loss of Weight & Appetite

PAST HISTORY:

1. Previous treatment

a) Drugs - Steriod therapy - Duration

b) Surgery - Endoscopic / External approach / Combined

2. H/o Immuno suppression

3. H/o Diabetes / Hypertension / IHD

PERSONAL HISTORY:

Smoking / Alcoholic / Snuff / Gardening

FAMILY HISTORY :

OCCUPATIONAL HISTORY :

1) GENERAL EXAMINATION :

Built :

Nourishment :

Anaemia :

Weight / BP / Temperature :

SYSTEMIC EXAMINATION

Cardiovascular system : Heart sounds / Murmur

Respiratory System :

Abdomen :

Central Nervous System :

LOCAL EXAMINATION

1. NOSE : Skin

External Contour

Nasolabial fold

Anterior Rhinoscopy :

Septum Deviated to R/L/Midline

Mass

Probing

Nasal Airway

Bleeding on touch

Nasal discharge

Posterior Rhinoscopy :

Mass

Discharge

Choanae / Eustachian Tube

2. ORBIT :

Proptosis

Acuity of vision

Movement of the eye ball

Lacrimation

Oedema of the eyes

Hypertelorism

3. ORAL CAVITY :

Oral mucosa

Teeth

Hard & Soft palatal ulcer

4. EXAMINATION OF CRANIAL NERVES :

5. EAR :

6. THROAT :

Indirect Laryngoscopic Examination

INVESTIGATIONS

Routine blood and urine tests

Blood sugar / urea / Lipid profile

Radiological Investigations

X-ray or Paranasal sinuses

& Nasopharynx

CT Scan of Nose and Sinuses

MRI

Diagnostic Nasal Endoscopy Findings

Histopathological Report

Fungal Culture Report

PROVISIONAL DIAGNOSIS: